

*FDA CTP - Third Party Governance of Industry-Sponsored
Tobacco Product Research: A Public Workshop*

March 20, 2013

A Matter of Record
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Min-U-Script® with Word Index

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2 CENTER FOR TOBACCO PRODUCTS
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10 Wednesday, March 20, 2013
11 8:30 a.m. to 12:50 p.m.
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1 P R O C E E D I N G S
2 (8:30 a.m.)
3 MS. DILLEY: We have a just a few people
4 checking in still, so we'll take another couple of
5 minutes, and then we'll get started.
6 Introduction
7 DR. ASHLEY: I think we may have a few
8 people continuing to wander in, but we're going to
9 go ahead and get started.
10 Welcome back to our second day of FDA's
11 public workshop on Third Party Governance of
12 Industry-Sponsored Tobacco Product Research.
13 Yesterday, we had a series of fruitful and what I
14 thought was very interesting discussions. We first
15 heard from Daniel Carpenter about the IOM
16 committee's deliberations and recommendations
17 regarding third-party governance. It's really
18 served to provide some useful context and to kind
19 of frame the topics and discussion over the two-day
20 workshop.
21 A couple of things I took out of that
22 directly was really the impact of the Swedish Match

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1 letter, which came to IOM and kind of got them
2 started on thinking about these issues and also,
3 really about their concern about vulnerable
4 subpopulations and the challenges in doing any kind
5 of studies related to vulnerable subpopulations.
6 We then heard from a range of interested
7 parties in the academic research and public health
8 communities about the challenges of conducting
9 industry-sponsored tobacco product research. We
10 heard a number of comments about the challenges of
11 history, the history of research being sponsored by
12 the tobacco industry and also differences between
13 general research areas and product-specific
14 research, and kind of the challenges in looking at
15 those two different aspects as we consider that.
16 And also, we heard some discussion about challenges
17 of really accepting industry funding to do research
18 in the academic communities and what that presented
19 for them.
20 We also heard two examples of independent
21 review that have been used in other arenas,
22 followed by a discussion of the aspects of those

<p style="text-align: right;">Page 5</p> <p>1 approaches. Some of those may or may not apply to 2 what we're doing here, but they were kind of 3 different things. They brought up a number of 4 things for us to consider.</p> <p>5 As the IOM noted, there's really no 6 independent entities to fulfill these roles for the 7 tobacco industry, so there's really not a good 8 example for us to basically say we will adopt that. 9 But we will try to use those two examples as things 10 we might learn some things from.</p> <p>11 We talked about concern with the challenge 12 of opening up data to the public and having the 13 transparency issue around data and how the public 14 may respond and how the public may evaluate data 15 and the challenges and the concerns about doing 16 that for an organization.</p> <p>17 Today, we'll be starting the meeting with a 18 public comment session, followed by a continuation 19 of the discussion of the challenges in conducting 20 industry-sponsored tobacco product research. I 21 look forward to continued discussions on the issue. 22 I'm now going to turn it back over to Abby</p>	<p style="text-align: right;">Page 7</p> <p>1 some new people in terms of the organization. 2 David's already given you the content of the 3 discussion today and a brief review of yesterday. 4 Most of you were here for that, and some of those 5 online, also, but I just want to go over a few 6 things.</p> <p>7 So in order to gather as much information as 8 possible, we have three different ways of doing 9 that. We have public comment period, and David 10 referenced we'll be doing that right after we go 11 over a few of the preliminaries. We also have 12 presentations today similar to yesterday. The 13 presenters will have around 10, 15 minutes of time 14 for their presentations, and then we'll take some 15 brief Q&A just for questions of clarity.</p> <p>16 Then there will also be after each 17 of -- well, the main panel today -- not after 18 public comment period, we don't Q&A after that. 19 But we do have Q&A at the end of the day at the end 20 of the panel.</p> <p>21 So we'll take a break after I think we have 22 two speakers initially, and then we have a series</p>
<p style="text-align: right;">Page 6</p> <p>1 Dilley. She's going to give us -- because we've 2 got some new folks in the audience, she's going to 3 kind of give us a little bit of what we heard 4 yesterday about kind of the ground rules of what 5 we're working under, and I'll let Abby take it from 6 here. Thank you.</p> <p>7 MS. DILLEY: Thanks, David.</p> <p>8 Good morning. My name is Abby Dilley, and I 9 work for an organization named RESOLVE, a nonprofit 10 organization based here in D.C. And my colleague 11 Beth Weaver and I, along with some of the CTP 12 staff, are here to help support what we hope will 13 be a productive second day of this workshop, and 14 really to help support the primary goals of this 15 session, which are to gather as much input and 16 information regarding the development of credible 17 research on modified-risk tobacco products and the 18 use of third-party governance structures for those 19 products, as well as a broader discussion of some 20 of the issues around research.</p> <p>21 So I just wanted to go over a couple of 22 things, as David mentioned, given that we do have</p>	<p style="text-align: right;">Page 8</p> <p>1 of five speakers. And I just want to remind people 2 on the agenda that there's a little typo in there. 3 I think we had a 45-minute break. We don't. We 4 have a 15-minute break so we have a little bit more 5 time for the series of the last section of 6 presenters on that panel. And then, again, we'll 7 have approximately 45 minutes to an hour for a 8 question-and-answer period. And then we'll have 9 some final comments, some thank yous, and we'll 10 adjourn no later than 1:00.</p> <p>11 So my role as moderator is to keep us on 12 track and on time and on task. And we have the 13 lights for the speakers to just give them a range 14 of their time, and that seemed to work very well 15 yesterday, and then also, to do some follow-up 16 questions. As I mentioned yesterday, I've done 17 some work in this area. I know some of the issues, 18 but I'm certainly not an expert. So please correct 19 me if I repeat a question or from the e-mail; 20 certainly feel free to follow up.</p> <p>21 Those of you who are submitting questions, 22 we strongly encourage you to do that. We did take</p>

<p style="text-align: right;">Page 9</p> <p>1 questions from e-mails yesterday, so we'd like to 2 continue to do that so that, again, all for the 3 purpose of gathering as much information and input, 4 just so we can be sure to get as much information 5 as possible.</p> <p>6 Similar to yesterday, we'd like to use some 7 just basic meeting protocols in terms of staying on 8 topic and task around these issues. Be brief and 9 to the point with questions. I thought people did 10 great yesterday. Again, we're really trying to get 11 to as many questions. I don't think we ever ran 12 out of -- maybe there were one or two times where 13 people had a couple of additional questions, but I 14 think we got to as many as we could yesterday.</p> <p>15 Again, if you do have additional comments or 16 questions that we don't get to, there are cards 17 over there to submit some additional questions. 18 There's also going to be, as follow-up to this 19 meeting, the webcast will be archived. There will 20 be a transcript, and then there will also be a 21 public docket that will be opened, and people can 22 submit additional comments when that docket is open</p>	<p style="text-align: right;">Page 11</p> <p>1 yesterday. Raquel Ortiz is in the back. If 2 there's any interest in setting up interviews with 3 CTP staff or FDA staff, she's the person to talk 4 with to go through the appropriate channels to do 5 that. For others, certainly, you can talk to 6 others as you want to. But, again, we would ask 7 that you do that at the break and outside the room 8 so we can keep the discussion focused inside the 9 room.</p> <p>10 Hopefully, when you came through 11 yesterday -- today -- that you picked up your 12 materials. There were slides from yesterday, and 13 now there are slides for today, the presenters this 14 morning, out there. So if you haven't gotten 15 those, there are copies out there.</p> <p>16 There's also the agenda, and then the 17 feedback form. So would appreciate feedback from 18 anyone and everyone who could provide that. And 19 the box up here again is for those forms, so please 20 do fill those out.</p> <p>21 Any questions about our agenda today? 22 (No response.)</p>
<p style="text-align: right;">Page 10</p> <p>1 on this topic. So, again, trying to encourage as 2 much input as possible.</p> <p>3 Lastly, just being respectful of everyone's 4 time. And certainly in keeping with yesterday, 5 there were certainly some strong opinions around 6 this topic and the issues associated with that, and 7 I think we can do it in a respectful manner. That 8 I think was certainly the case yesterday and 9 continue that today.</p> <p>10 Just in terms of helping, encourage 11 everybody being able to hear the conversation, to 12 turn your cell phones off, any electronic devices. 13 If you haven't already done that, we'd appreciate 14 it.</p> <p>15 Then also, if you have conversations with 16 people, if you could do that outside or wait for a 17 break. It's just distracting when people are 18 trying to hear the presentations, and just to make 19 sure we're having one conversation in the room, it 20 helps quite a bit to do that.</p> <p>21 I don't think there are members of the media 22 here, but if there are, similar structure to</p>	<p style="text-align: right;">Page 12</p> <p>1 Public Comment Session</p> <p>2 MS. DILLEY: So as we mentioned, we'll move 3 right into the public comments section of the 4 agenda. And we have three people who 5 pre-registered per the notice today. We're going 6 to have them come up here and use the microphone up 7 here. They'll have 10 minutes per person, so 8 they'll have the light system as well. It'll give 9 you a yellow and a red as you get close to your 10 10 minutes, if they go to that length of time.</p> <p>11 I think the first speaker that was signed up 12 is Sharon Eubanks. Sharon. Okay. You're here. 13 Good. So come on up, and we will start the public 14 comment period. Thank you for coming.</p> <p>15 MS. EUBANKS: Good morning. I'm here to 16 read letters that Ruth Malone provided, Ruth 17 Malone, UCSF, department of social and behavioral 18 sciences, directed to Center for Tobacco Products, 19 Food and Drug Administration, dated January 20, 20 2013.</p> <p>21 "Dear Colleagues, I was very surprised to be 22 invited to present as part of an FDA sponsored,</p>

<p style="text-align: right;">Page 13</p> <p>1 quote, unquote, 'facilitated dialogue panel' also 2 featuring tobacco industry representatives, which 3 would be focused on the topic of industry-funded 4 research. This very type of industry engagement 5 with senior public health officials is straight out 6 of the tobacco companies' public relations, quote, 7 unquote, 'corporate social responsibility 8 playbook,' and was something that at least one 9 tobacco company anticipated as a favorable result 10 of FDA legislation." 11 I'm going to omit the footnotes for purposes 12 of time. 13 "Such dialogues have been part of this and 14 earlier industry public relations campaigns. 15 Public health authorities and scientists, to say 16 nothing of the federal agency charged with 17 regulating this industry, should not lend their 18 legitimacy to the tobacco companies' efforts to 19 position themselves as socially responsible. 20 "I would be very willing to come to 21 Rockville and share my perspectives with the FDA on 22 the issue of third party and tobacco products</p>	<p style="text-align: right;">Page 15</p> <p>1 promote the use of cigarettes, their single most 2 deadly product. While the companies may have an 3 interest in reducing the numbers who die 4 prematurely from using their products so that they 5 will live to purchase more of them, they have never 6 indicated any willingness to pull from the market 7 the products that kill half their longtime users 8 and continue to be sold. Absent such willingness, 9 the practical goals of public health and the 10 tobacco industry are in direct conflict. No 11 dialogue will change that. 12 "Second, any such discussion among 13 stakeholders would require minimal level of mutual 14 understanding about the nature and purpose of 15 science. However, a large body of academic 16 research, based on the industry's own internal 17 documents, as well as federal Judge Gladys 18 Kessler's extensive findings of fact in the 19 successful U.S. Department of Justice racketeering 20 case against the major tobacco companies 21 demonstrates that research is an arena in which the 22 tobacco industry is particularly untrustworthy.</p>
<p style="text-align: right;">Page 14</p> <p>1 research. However, I cannot in good conscience 2 participate as a panelist in this facilitated 3 dialogue with the tobacco industry. Further, I 4 strongly urge that other researchers from the 5 public health community decline participation on 6 such panels. The FDA should consider other means 7 of determining a suitable framework for addressing 8 the many issues related to industry-funded 9 research. 10 "While this is clearly an issue about which 11 I have thought and written extensively, I think 12 this meeting as currently envisioned is a very bad 13 idea. My reasons are, first, involving the tobacco 14 companies as stakeholders on the panel with the 15 public health community in this way suggests that 16 all parties share a common or at least congruent 17 role. This is a flawed assumption. 18 "Public health advocates, and presumably, 19 the FDA, have a stake in saving lives. Tobacco 20 companies have a stake in protecting profits. The 21 research evidence has repeatedly demonstrated that 22 they will do whatever it takes to continue to</p>	<p style="text-align: right;">Page 16</p> <p>1 "This fact is also repeatedly noted in the 2 Institute of Medicine's report on scientific 3 standards for studies on modified-risk tobacco 4 products. As the Kessler decision found, the 5 tobacco industry engaged in a conspiracy to cover 6 up and distort the evidence of their product's 7 harmfulness, and they have a long track record of 8 egregious manipulation of science. The courts also 9 found that this behavior is continuing and likely 10 to continue in the future. I see no reason to 11 differ with this conclusion. 12 "For this very reason, Tobacco Control, the 13 journal that I edit, and other reputable scientific 14 journals, including Plus Medicine, no longer 15 publish tobacco-industry-funded research. To 16 engage the industry as a legitimate partner in the 17 discussion of how we deal with industry science is 18 to ignore this large body of evidence. 19 "Third, as noted briefly above, such 20 engagements have long been envisioned by tobacco 21 companies as facilitating their image reform 22 efforts while creating divisions within the tobacco</p>

<p style="text-align: right;">Page 17</p> <p>1 control community. As we demonstrated in our 2 papers examining Philip Morris' support for FDA 3 regulation of tobacco products and its development 4 of Project Sunrise, which sought to create and 5 exploit divisions within tobacco control, 6 engagement with public health organizations allows 7 tobacco companies to position themselves as 8 reasonable and responsible and position those who 9 refuse to engage as extremists.</p> <p>10 "In fact, shortly after the failure of a 11 previous bill giving FDA authority to regulate 12 tobacco, top Philip Morris executives were 13 exploiting public speaking opportunities in which 14 they falsely claimed to have partnered with leading 15 public health organizations in supporting 16 regulation. This is precisely the type of mileage 17 tobacco companies can achieve from engaging in 18 facilitated dialogues such as those envisioned by 19 the FDA.</p> <p>20 "Fourth, tobacco industry demoralization is 21 a key part of successful tobacco control efforts. 22 Convening a meeting of this sort undermines those</p>	<p style="text-align: right;">Page 19</p> <p>1 however, required to facilitate dialogue as though 2 it were acting as a neutral mediator between two 3 parties with equally valid but divergent interests.</p> <p>4 "In positioning itself as some sort of 5 neutral party, FDA is unwittingly acting as an 6 agent for the tobacco industry's public relations 7 initiatives and undermining a strong tobacco 8 control strategy. This is very problematic, and 9 those of us who have spent more than a decade 10 researching industry strategies, enormously naive.</p> <p>11 "For those reasons, I am declining to 12 participate in this meeting and urging my 13 colleagues to do the same. Sincerely, signed, Ruth 14 E. Malone, RN, PhD, FAAN, professor and chair, 15 Department of Social and Behavioral Sciences, 16 editor, Tobacco Control."</p> <p>17 Letter dated February 6, 2013 from Ruth 18 Malone, University of California San Francisco, 19 directed to Lawrence Dayton, MD, director, Center 20 for Tobacco Products.</p> <p>21 "Dear Dr. Dayton and tobacco control 22 colleagues, I do appreciate the attempts of the</p>
<p style="text-align: right;">Page 18</p> <p>1 critically important efforts by creating a forum 2 for re-legitimization through association with 3 respected public health agencies and leaders. 4 Lending the FDA imprimatur to a public meeting 5 featuring tobacco company speakers suggests that 6 something has indeed changed and the industry is no 7 longer harming people through its promotion of 8 deadly products, but this is patently untrue.</p> <p>9 "And as we recently showed in an extensive 10 review, a robust body of evidence supports tobacco 11 industry demoralization as an effective 12 population-level tobacco control strategy that 13 contributes to reduced smoking prevalence among 14 young people, reduced youth smoking initiation, 15 increased intentions to quit, and reduced perceived 16 peer smoking prevalence. It is very puzzling that 17 the FDA would act in a way that undermines this 18 important work.</p> <p>19 "The FDA may be required to interact with 20 industry for the purposes of discussing proposed 21 regulation of tobacco products and what tobacco 22 companies must do to comply. The FDA is not,</p>	<p style="text-align: right;">Page 20</p> <p>1 Center for Tobacco Products to respond to the 2 issues raised in my previous letter declining the 3 invitation to be part of the planned dialogues 4 panel with the tobacco industry. While I applaud 5 the dropping of the facilitated dialogues meeting 6 characterization, the proposed revised format, 7 which clusters invited presenters from government, 8 academics, and public health representatives on 9 day 1, followed by invited presentations from the 10 tobacco industry on day 2, does not adequately 11 address the substantive issues raised by my letter. 12 It remains the same meeting with the same agenda 13 and purpose, merely rearranging the program.</p> <p>14 "Therefore, I must again respectfully and 15 regretfully decline your invitation to attend this 16 particular meeting. The first point raised in my 17 previous letter related to regarding tobacco 18 companies as equivalent stakeholders with public 19 health. I see nothing in the revised format that 20 changes this since public health and tobacco 21 company representatives continue to be placed on 22 the same meeting agenda as co-equals, albeit now on</p>

<p style="text-align: right;">Page 21</p> <p>1 different days.</p> <p>2 "Tobacco companies are stakeholders only in</p> <p>3 the promotion of tobacco product use, not promoting</p> <p>4 public health, which is the purpose of the Family</p> <p>5 Smoking Prevention and Tobacco Control Act. While</p> <p>6 the tobacco companies have every right to express</p> <p>7 their opinions and submit materials for the FDA's</p> <p>8 consideration, you are not required to treat the</p> <p>9 regulated industry equally as though they had</p> <p>10 demonstrated materially that they share the goals</p> <p>11 of protecting public health. They have not done</p> <p>12 so.</p> <p>13 "My second point addressed the absence of</p> <p>14 mutual understanding of what constitutes legitimate</p> <p>15 science and ethical conduct in science. The</p> <p>16 revised format does nothing to reassure me that a</p> <p>17 reasonably comprehensive understanding of Judge</p> <p>18 Kessler's extensive findings of fact in her ruling</p> <p>19 in the Department of Justice RICO case, USA v.</p> <p>20 Philip Morris, et al., is now informing the FDA's</p> <p>21 activities or has been incorporated into the</p> <p>22 agenda. These findings of fact are clearly</p>	<p style="text-align: right;">Page 23</p> <p>1 facilitated dialogue or public workshop seems less</p> <p>2 important in this regard than the fact that it is</p> <p>3 still one in the same meeting with chairs</p> <p>4 rearranged and did not have to happen this way. It</p> <p>5 is disturbing when public health agencies</p> <p>6 contribute to such divisions.</p> <p>7 "Fourth, the tobacco companies have every</p> <p>8 right to make comments, and one would expect them</p> <p>9 to do so. And the FDA has a responsibility to give</p> <p>10 comments from the regulated industry fair</p> <p>11 consideration. But legal colleagues have advised</p> <p>12 me that while the FDA is certainly permitted to</p> <p>13 invite industry speakers to present at a meeting on</p> <p>14 how to deal with industry science, there is no</p> <p>15 legal requirement that they do so; and in the</p> <p>16 absence of such a requirement, I continue to</p> <p>17 question why FDA feels it must give the industry a</p> <p>18 stage. They certainly do not have such status,</p> <p>19 even on the TPSAC where they are separated by being</p> <p>20 nonvoting members. Your legal mandate is to</p> <p>21 regulate the industry in the service of public</p> <p>22 health, not to provide it a podium for its</p>
<p style="text-align: right;">Page 22</p> <p>1 relevant for the FDA to consider in its decision</p> <p>2 making, as indicated by the fact that Congress</p> <p>3 included three findings, numbers 47, 48, and 49,</p> <p>4 from Judge Kessler's ruling in the Family Smoking</p> <p>5 Prevention and Tobacco Control Act.</p> <p>6 "While there has been a proliferation of</p> <p>7 smaller tobacco and nicotine device companies that</p> <p>8 are not defendants in the RICO case, the fact</p> <p>9 remains that the major cigarette companies continue</p> <p>10 to dominate the market, both in this country and in</p> <p>11 the world; that they continue patterns of</p> <p>12 acquisition of the more promising smaller</p> <p>13 companies, and that the federal court found their</p> <p>14 fraudulent conduct was continuing and likely to</p> <p>15 continue into the future. This is highly material</p> <p>16 to any discussion of industry-sponsored tobacco</p> <p>17 products research.</p> <p>18 "Third, it is clear that this meeting has</p> <p>19 indeed has the effect of contributing to divisions</p> <p>20 within tobacco control, as some invitees now feel</p> <p>21 they must attend and others, including me, feel</p> <p>22 they must decline. Whether it is officially called</p>	<p style="text-align: right;">Page 24</p> <p>1 propaganda.</p> <p>2 "The leading tobacco companies have</p> <p>3 repeatedly demonstrated antipathy to the FDA,</p> <p>4 creating multiple obstacles to its ability to carry</p> <p>5 out its responsibilities for implementing the</p> <p>6 Family Smoking Prevention and Tobacco Control Act.</p> <p>7 Far from being equal stakeholders in the FDA's</p> <p>8 mission, some have sued to block implementation of</p> <p>9 health warning labels, and others are opening</p> <p>10 flouting FDA's regulations, banning the use of</p> <p>11 light and mild and other descriptors, simply</p> <p>12 replacing these words with color coding. These are</p> <p>13 only the most obvious examples.</p> <p>14 "Our current moment does not call for a</p> <p>15 cautious, prolonged and exorbitantly expensive</p> <p>16 replay of the infamous safer cigarette debacles of</p> <p>17 the past in which the tobacco industry partnered</p> <p>18 with health researchers in a cynical ploy to buy</p> <p>19 decades' more time at the expense of millions of</p> <p>20 lives.</p> <p>21 "What is called for now is the political</p> <p>22 courage to acknowledge and incorporate decisively</p>

<p style="text-align: right;">Page 25</p> <p>1 in policy planning the vast evidence demonstrating 2 that tobacco companies are untrustworthy; hence, 3 the need for strong, rapidly enacted and well 4 enforced regulations to protect the public from 5 suffering another century of tobacco-caused deaths. 6 "What is called for now is informed, savvy 7 leadership. I urge the FDA to provide it. Please 8 enter this letter with the earlier letter to which 9 it refers into the record of the meeting. If 10 necessarily, I would be willing to arrange for 11 someone to attend and read these into the record. 12 "Thank you for your consideration. 13 Sincerely, Ruth E. Malone, RN, PhD, FAAN, professor 14 and chair, Department of Social and Behavioral 15 Sciences, editor in chief, tobacco control." 16 Dr. Malone asked me to let everyone know 17 that she hopes that this is a successful endeavor. 18 Thank you. 19 MS. DILLEY: Thank you. 20 The next speaker is Elaine Keller. 21 We're not taking questions. This is not a 22 Q&A period.</p>	<p style="text-align: right;">Page 27</p> <p>1 dysfunctional. 2 Those who choose to disbelieve the 2007 3 Royal College of Physicians' report and the 2001 4 Institute of Medicine report need only take a look 5 at the adult smoking prevalence rates between 1990 6 and 2009 to see that the abstinence only approach 7 does not work for everyone. 8 The effects of nicotine dependence are quite 9 different from other substances. Nicotine does not 10 cause accidents, aggressive behavior, loss of 11 inhibition, or impaired decision making. 12 Furthermore, these other substances can cause 13 direct damage to the body such as liver disease, 14 nerve disorders and dementia, whereas nicotine does 15 very little direct damage to the body when it is 16 delivered in some way other than inhaling smoke. 17 During the workshops and public hearings 18 held by the FDA, we have seen overwhelming 19 scientific evidence that smokeless tobacco use has 20 a much lower risk than smoking, yet the tobacco 21 control industry persists in publishing grossly 22 misleading statements such as smokeless tobacco is</p>
<p style="text-align: right;">Page 26</p> <p>1 MS. KELLER: Good morning. I'm Elaine 2 Keller, and even though I serve as president of an 3 advocacy organization, CASAA, today I'm testifying 4 as a private citizen. 5 One of the questions to be addressed in this 6 FDA workshop was what are the barriers to 7 implementing third-party governance of 8 industry-sponsored tobacco product research and how 9 can these barriers be overcome. These questions 10 become moot if no research is conducted, so I'm 11 going to reframe the issue. 12 What are the barriers to saving the lives of 13 smokers? After all, isn't saving lives the 14 ultimate goal of making modified-risk tobacco 15 products available to smokers? 16 One of the greatest barriers to saving the 17 lives of smokers is the strong opinion of anti- 18 tobacco extremists that there is no need for MRTPs. 19 This opinion is predicated on belief in a number of 20 falsehoods. There is strong evidence that a 21 significant number of smokers will never be able to 22 become abstinent from nicotine without becoming</p>	<p style="text-align: right;">Page 28</p> <p>1 not a safe alternative to cigarettes. 2 Research definitely shows that there is a 3 dose response relationship between diseases and 4 volume of smoking. Those who start smoking with 5 smoking tend to reduce the number of cigarettes 6 smoked when they add another source of nicotine. 7 Many of those who completely stop smoking go 8 through a period of dual use. Smoking reduction is 9 proven to be an effective way for some smokers to 10 quit, especially so when they begin to replace 11 their cigarettes with a lower risk source of 12 nicotine. 13 As long as the above myths as left 14 uncorrected, the perception will persist among 15 anti-tobacco extremists that there is no need to 16 create any MRTPs. Unfortunately, nicotine 17 abstinence is unworkable for millions of smokers. 18 MRTPs may be the only practical solution for the 19 millions of smokers trapped in the Sophie's choice 20 of quit or die. 21 The Department of Health and Human Services 22 needs to set the record straight. The FDA, CDC and</p>

<p style="text-align: right;">Page 29</p> <p>1 NIH websites that misinform the public about 2 nicotine and about relative risks of tobacco 3 products needs to be revised to present the truth, 4 the whole truth, and nothing but the truth. 5 In addition, since this misinformation has 6 been deeply entrenched, the FDA needs to pave the 7 way for public acceptance of the need for and 8 effectiveness of substitutes for smoking by 9 providing accurate information about nicotine, 10 smoking, other tobacco products, and the risks of 11 each. The FDA and other government agencies should 12 launch a public information campaign that includes 13 the points you see here. 14 In the 2000 National Health interview 15 survey, pharmaceutical products were successfully 16 used to quit by 0 to 35 percent of smokers, while 17 switching to a smokeless tobacco product had a 18 73 percent success rate. 19 Let's look at the barriers to making MRTPs 20 available. Consumers are starting to have a strong 21 suspicion that this game is rigged. We see so much 22 false health information about tobacco and nicotine</p>	<p style="text-align: right;">Page 31</p> <p>1 scientific and health research to refuse to accept 2 tobacco funding. Without the cooperation of these 3 organizations, how can the required clinical trials 4 be conducted? And even if the tobacco industry 5 managed to conduct clinical trials without the 6 participation of the organizations that currently 7 conduct research for pharmaceutical companies, 8 where would the watchdogs for third-party 9 governance come from? 10 To actually save lives, FDA needs to remove 11 the barriers to complying with the requirements for 12 MRTP approval. To make sure that human testing can 13 be conducted, the government needs to enlist the 14 cooperation of universities, private research 15 organizations, and health-related nonprofits, as 16 well as the cooperation of other divisions of the 17 government in getting the research done. It can 18 only hurt public health if organizations refuse to 19 participate in the research required to answer the 20 most important questions. These types of projects 21 necessarily include tobacco industry involvement. 22 The government might give serious thought to</p>
<p style="text-align: right;">Page 30</p> <p>1 spread across DHHS websites that we've begun to 2 question everything. We have stopped taking 3 abstracts at face value and insist on reading the 4 entire article, and then draw our own conclusions. 5 We have seen many journal articles where there is a 6 mismatch between the results of the research and 7 the way the findings are reported. And perhaps 8 most disheartening, much of this research is 9 funded, at least in part, by the federal 10 government. 11 The requirement for extensive testing of 12 tobacco products that we already know are lower in 13 risk than smoking is wasteful and is a barrier to 14 saving the lives of smokers. We have to wonder 15 whether the bar has been set so high on purpose. 16 Making the requirements too costly and too time 17 consuming allows the FDA to claim that they 18 complied with Section 911 without actually 19 approving a single product to be marketed as a 20 MRTP. 21 Anti-tobacco extremists have convinced most 22 academics and independent companies that conduct</p>	<p style="text-align: right;">Page 32</p> <p>1 refusing to award any projects at all to 2 organizations that refuse to be cooperative. 3 On the other hand, the greatest threat to 4 consumers and honest research comes from some 5 factions of the tobacco control industry. We 6 believe watchdogs are necessary to prevent anti- 7 tobacco extremists from skewing the data or from 8 reporting the results in such a way so as to 9 sabotage the development and approval of MRTPs. 10 Third-party governance does not mean that 11 tobacco industry research should be replaced with 12 equally biased anti-tobacco research. The 13 manufacturers should be encouraged to outsource 14 research to independent researchers or provide 15 third-party audits wherever possible. But they 16 should not just allow those with opposing biases to 17 control the research. 18 One way to ensure objectivity in the 19 collection and reporting of data would be to 20 recruit as third-party watchdogs those health and 21 science experts who have never participated in 22 tobacco control.</p>

<p style="text-align: right;">Page 33</p> <p>1 Experience has shown consumers that we can't</p> <p>2 always trust that the tobacco control industry</p> <p>3 produces more honest research results than the</p> <p>4 tobacco industry. Let me give you a practical</p> <p>5 example. In 2009, FDA announced electronic</p> <p>6 cigarettes contained carcinogens and antifreeze. I</p> <p>7 had been smoke-free for three months when those</p> <p>8 reports were splashed across the media, and I very</p> <p>9 nearly decided it might be safer for me to go back</p> <p>10 to smoking.</p> <p>11 The researcher Carl V. Phillips has</p> <p>12 calculated that continuing to smoke for even two</p> <p>13 more months does more damage to health than</p> <p>14 switching to a smoke-free alternative and</p> <p>15 continuing to use it for the rest of one's life.</p> <p>16 If I had not stopped smoking four years ago, by</p> <p>17 now, I might have needed to drag around an oxygen</p> <p>18 tank wherever I go.</p> <p>19 Thank God, a few honest scientists spoke out</p> <p>20 and explained that the FDA's report was not the</p> <p>21 whole truth. Important information was left out.</p> <p>22 But how many smokers never saw the debunking</p>	<p style="text-align: right;">Page 35</p> <p>1 much.</p> <p>2 (Applause.)</p> <p>3 MS. DILLEY: All right. And our last public</p> <p>4 speaker today is Greg Conley. Is he here?</p> <p>5 MR. CONLEY: Good morning. I'm afraid that</p> <p>6 Sharon Eubanks stole my idea for my speech, so I'm</p> <p>7 going to have to wing it.</p> <p>8 (Laughter.)</p> <p>9 MR. CONLEY: My name is Gregory Conley, and</p> <p>10 I am here on behalf of the Consumer Advocates for</p> <p>11 Smoke-free Alternatives Association, known as</p> <p>12 CASAA. We are the leading U.S. advocate that</p> <p>13 represents consumers of low risk smoke-free</p> <p>14 alternatives to smoking, including electronic</p> <p>15 cigarettes and smokeless tobacco and other</p> <p>16 consumers how might someday switch to such</p> <p>17 products.</p> <p>18 We are an all-volunteer organization funded</p> <p>19 entirely by donations. Our organization does not</p> <p>20 take positions on the regulation of cigarettes or</p> <p>21 smoking, and therefore, all of my remarks should be</p> <p>22 interpreted as referring to research and regulation</p>
<p style="text-align: right;">Page 34</p> <p>1 articles and made the misinformed decision to</p> <p>2 continue smoking instead of switching? In the past</p> <p>3 four years, how many cases of COPD, lung cancer,</p> <p>4 heart attacks and strokes occurred that would have</p> <p>5 been prevented had the FDA told the public the</p> <p>6 whole truth?</p> <p>7 Well, I guess this doesn't need a whole lot</p> <p>8 of explanation because we've already talked about</p> <p>9 the fact that we know that smokeless tobacco is a</p> <p>10 lot less harmful than smoking, so this is not true.</p> <p>11 And this message is from a fellow consumer. She's</p> <p>12 a 61-year-old grandmother and engineer who smoked a</p> <p>13 pack a day for 43 years and tried to quit six times</p> <p>14 with patches, one time with gum, a thousand times</p> <p>15 by cold turkey, and is on Prozac and is terrified</p> <p>16 of Chantix.</p> <p>17 She says, "I finally quit this January 1st</p> <p>18 after nine months of learning to vape, learning the</p> <p>19 equipment, and investigating flavors."</p> <p>20 I'll accept any questions you might have.</p> <p>21 MS. DILLEY: Thank you. We're not doing any</p> <p>22 questions after public comments, but thank you very</p>	<p style="text-align: right;">Page 36</p> <p>1 of smoke-free products and regulation about tobacco</p> <p>2 harm reduction.</p> <p>3 Research on tobacco harm reduction and</p> <p>4 smoke-free alternatives should focus on benefitting</p> <p>5 the primary stakeholder, the consumer. Therefore,</p> <p>6 we support the principle of encouraging research</p> <p>7 that is controlled by third parties who are</p> <p>8 primarily interested in informing and benefitting</p> <p>9 consumers. However, we believe that the greatest</p> <p>10 concerns about research that is not done honestly</p> <p>11 or is done in ways that do not support the public</p> <p>12 interest do not actually relate to the tobacco or</p> <p>13 e-cigarette industries.</p> <p>14 Recent research on these products, a</p> <p>15 significant body of which was conducted or directly</p> <p>16 funded by the tobacco or E cigarette industries,</p> <p>17 has been in close alignment with the public</p> <p>18 interest. Specifically, it has been honest</p> <p>19 research that has pursued ways to improve the</p> <p>20 health and well-being of tobacco and nicotine</p> <p>21 consumers.</p> <p>22 By contrast, there is serious concern about</p>

<p style="text-align: right;">Page 37</p> <p>1 research that is conducted and sponsored by another 2 special interest group, the tobacco control 3 industry, the coalition of organizations and 4 individuals who are dedicated to the elimination of 5 all tobacco and nicotine use. Because honest 6 consumer-oriented research tends to support tobacco 7 harm reduction and because tobacco harm reduction 8 is a threat to the tobacco control industry's 9 business model, they have actively promoted 10 scientific disinformation about smoke-free 11 alternatives with the intent of misleading 12 consumers into not making the switch.</p> <p>13 This has been documented by researchers for 14 over a decade, and our own current research and 15 publications document that this disinformation 16 campaign continues. Thus redirecting some research 17 away from the manufacturer's control and to the 18 control of those who are specifically concerned 19 about consumer choices and welfare might 20 theoretically offer some modest benefits for the 21 public interest.</p> <p>22 To facilitate this, it is important to push</p>	<p style="text-align: right;">Page 39</p> <p>1 based entirely on events that occurred many years 2 before I was born -- and I apologize if that ages 3 anyone in the audience -- actions taken by people 4 who have long since retired or died.</p> <p>5 The industry's interests are not perfectly 6 aligned with those of consumers. But the public 7 interest can and should be served by the FSPTCA's 8 already extensive FDA regulatory oversight. A 9 large portion of industry-funded research can be 10 carried out by independent researchers who are 11 primarily concerned about consumers and about doing 12 the best possible science. In addition, the few 13 in-house industry research operations appear to be 14 very interested in doing the best possible science 15 and in considering the health of consumers, even 16 when it does align perfectly with the maximization 17 of profits.</p> <p>18 Thus, we believe that the public interest 19 could be served by the creation of some consumer- 20 oriented, third-party institutions that conduct 21 research that was funded by manufacturers. 22 However, the status quo with respect to</p>
<p style="text-align: right;">Page 38</p> <p>1 back against the efforts to vilify any honest 2 independent researcher who accepts industry 3 funding, but redirecting research away from the 4 control of the tobacco control industry would be 5 enormously beneficial for consumers and the public 6 interest. The worst possible scenario would be to 7 use the principle of third-party governance of 8 research to put more research under the control of 9 anti-tobacco researchers who support an extremist 10 anti-tobacco harm reduction agenda that threatens 11 the health and welfare of consumers.</p> <p>12 The claims that the tobacco industry engages 13 in dishonest research are based on ancient history. 14 Recent research conducted and sponsored by the 15 several tobacco companies who are actively pursuing 16 tobacco harm reduction as well as e-cigarette 17 companies that have started to support research 18 appears to be honest and objective science.</p> <p>19 When someone makes claims about dishonest 20 research from the tobacco industry, they never 21 identify any recent example of ethical misconduct 22 or even bad research. Instead, their claims are</p>	<p style="text-align: right;">Page 40</p> <p>1 manufacturer-sponsored research is actually closely 2 aligned with the public interest, and, thus, no 3 major changes are demanded.</p> <p>4 By contrast, anti-tobacco activists have a 5 consistent record of publishing false and 6 misleading claims meant to discourage would-be 7 smokers from using low risk alternatives instead. 8 This extends to the scientific research they 9 conduct or control through their vast funding 10 network.</p> <p>11 Unlike the allegations about manufacturer 12 opposing hidden manipulation of science, which are 13 based on speculation and innuendo, it is easy to 14 observe misleading research coming from anti- 15 tobacco activists. Common tactics include 16 suggesting that trivial risks and exposures from 17 smoke-free products, which have no serious health 18 consequences, are similar to the risks of smoking; 19 denying the existence of the overwhelming evidence 20 about the efficacy and effectiveness of tobacco 21 harm reduction products; and, lastly, starting with 22 the premise that tobacco harm reduction is bad and</p>

<p style="text-align: right;">Page 41</p> <p>1 merely reporting that premise as if it were the 2 result of a study.</p> <p>3 Researchers have documented that these and 4 other anti-tobacco harm reduction lies from tobacco 5 control were common a decade ago, and they have 6 increased in volume since then. Frequently, they 7 appear in journal articles and other research 8 papers. CASAA has a blog that is specifically 9 devoted to identifying this misleading research 10 that runs contrary to the public interest. We 11 analyze several examples every week and are forced 12 to ignore many others due to the sheer volume.</p> <p>13 The goal of third-party governance is to 14 take control of research out of the hands of 15 special interests who are likely to bias the 16 science and otherwise act contrary to the public 17 interest. We understand that the FDA does not have 18 any authority to redirect funds away from this 19 misleading and harmful effort by anti-tobacco harm 20 reduction advocates, and we would not advocate for 21 the violation of free speech rights that such a 22 government confiscation would entail.</p>	<p style="text-align: right;">Page 43</p> <p>1 comment period. Thanks again to all the people who 2 signed up for public comment.</p> <p>3 So we'll take just a pause while we get 4 Scott situated up here, who's our first speaker. 5 We're transitioning now into the final segment of 6 the meeting, which is to continue the discussion 7 around challenges in conducting industry-sponsored 8 research. And we begin with Scott Ballin who is a 9 health policy consultant.</p> <p>10 Presentation – Scott Ballin 11 MR. BALLIN: Thank you, Abby. 12 I also want to first thank the agency for 13 the opportunity to be here today and also to extend 14 my best to the new director of the Center who I've 15 known for many, many years, even going back before 16 his involvement in tobacco, so that's a long time. 17 I also want to commend the agency for continuing to 18 hold workshops and meetings like this, where there 19 can be exchanges of ideas and new opportunities 20 explored that are so important in shaping policy 21 and decisions as we move forward, and what is to 22 me -- and I've said this for a couple years now.</p>
<p style="text-align: right;">Page 42</p> <p>1 However, the spirit of third-party 2 governance says that the FDA, and DHSS more 3 generally, should avoid directing any additional 4 research funding towards these activists and 5 activist organizations. If there is an opportunity 6 to direct research funds, whether they come from 7 manufacturers' fees and contributions or some other 8 source, to third parties who will do honest science 9 that is actually in the public interest of 10 consumers and not support an anti-harm reduction or 11 otherwise anti-consumer prohibitionist agenda, this 12 would probably have some benefit. However, the 13 current research practices of manufacturers are not 14 actually very far from this scenario.</p> <p>15 To reiterate, the worst possible scenario in 16 terms of public health, consumer well-being and 17 honest science would be to transfer more research 18 to the control of anti-tobacco activists.</p> <p>19 That concludes my speech, and I thank you 20 all for joining us today. 21 (Applause.) 22 MS. DILLEY: That concludes the public</p>	<p style="text-align: right;">Page 44</p> <p>1 This is a new era. As soon as FDA assumed 2 regulatory authority over tobacco, that changed the 3 dynamics of the discussion.</p> <p>4 I'm not a scientist, and I'm not a 5 researcher, but I hope to bring some perspectives 6 to this discussion based on 30 years plus of being 7 involved in tobacco control and public health 8 initiatives on tobacco. And those of you who know 9 me know that I've been advocating more recently the 10 fact that we really do need to be focused on a more 11 broader agenda in developing a more coherent and 12 rational approach to regulating not just tobacco 13 but nicotine products as well as alternative 14 products.</p> <p>15 There's been a sort of schizophrenia here at 16 the agency for years with a lot of the NRTs being 17 over at CDER, and now we have this new center. And 18 I've written quite a bit about this. And I think 19 we should not lose sight of the fact that this is a 20 bigger issue than just the narrow discussions we're 21 having with respect to tobacco. 22 I recognize that there are some -- and</p>

<p style="text-align: right;">Page 45</p> <p>1 you've heard some of this today -- who do not think 2 that any dialogue or engagement with the tobacco 3 industry, as we refer to them, is either 4 appropriate or beneficial, even in the scientific 5 arena. And one such critic recently told the 6 Washington Post, the industry is not a stakeholder. 7 And I respectfully disagree and think that this is 8 in this new era of regulatory oversight -- we now 9 have the opportunity to ensure that the industry's 10 behaviors will never be repeated.</p> <p>11 The Chinese general -- and I think many have 12 heard this expression before -- made the comment 13 that "Keep your friends close and your enemies 14 closer." And I think this is a perfect example 15 where we need to be watching the industry on a 16 regular basis, involving them directly in 17 discussions. I'm not talking about negotiations. 18 I'm talking about actually face-to-face dialogues 19 such as this meeting that's taking place.</p> <p>20 I think the IOM was correct in its report to 21 raise awareness that based on the industry's past 22 behaviors, there's reason to be wary and cautious</p>	<p style="text-align: right;">Page 47</p> <p>1 company -- who seeks approval from the FDA for an 2 MRTP.</p> <p>3 Along those same lines, I want to point out 4 that it's no longer so easy to define the tobacco 5 industry as well as the use of the word "tobacco" 6 as it was in the '70s, '80s and '90s, and it will 7 become increasingly difficult to do so. We need a 8 serious reconsideration of the terms that we are 9 using. The focus should be more on the science and 10 also on the products that are being developed and 11 less on who's making them. I mean, we could get 12 rid of the entire tobacco industry and still have a 13 lot of chaos out there. We have to begin to break 14 this down and approach it differently.</p> <p>15 It's not again just about tobacco. It's 16 about nicotine products as well. It's not so 17 inconceivable that a pharmaceutical company, a 18 device company, a biotech company will produce an 19 MRTP, or even a food company that deals with 20 agricultural-based products and science on a 21 regular basis who might apply its technologies into 22 developing and producing an innovative very</p>
<p style="text-align: right;">Page 46</p> <p>1 as we move forward, as their past actions have, 2 quote, "Resulted in significant distrust of the 3 tobacco industry."</p> <p>4 Yet at the same time, the IOM recognized it 5 will be the manufacturers, broadly speaking -- and 6 again, I'm not just talking about traditional 7 tobacco manufacturers -- who will have the burden 8 of producing scientific evidence about the MRTP 9 products that will be developed and produced. And 10 so their involvement is obviously going to be 11 required and essential in this process.</p> <p>12 After raising the yellow flag of 13 caution -- or maybe I should say a red flag -- the 14 IOM goes on to say, "Regulatory policies also 15 should seek to promote the meaningful involvement 16 of stakeholders that include the tobacco industry, 17 academic researchers, public health advocates, and 18 the public as well." That includes consumers. And 19 I would suggest that the statement be broadened to 20 be specifically inclusive of any manufacturer, 21 traditional tobacco companies or others -- it may 22 be a biotech company; it may be a pharmaceutical</p>	<p style="text-align: right;">Page 48</p> <p>1 low-risk product. That's very feasible.</p> <p>2 Traditional tobacco companies are themselves 3 expanding their portfolios that include a spectrum 4 of tobacco, nicotine, and alternative products. So 5 we have to begin to think outside the box a little 6 bit as we have these kinds of discussions as we 7 move forward.</p> <p>8 I also believe that had the Institute of 9 Medicine had the time and had not been constrained 10 by some of the requirements within the statutory 11 mandate, that the report could have been further 12 enhanced by making site visits to all the tobacco 13 companies who they were concerned about and raising 14 red flags about to gather more information, that 15 may have actually helped in the process of putting 16 the final report together. And I think that was a 17 missed opportunity, and that is again why I think 18 there needs to be more engagement, and not just 19 from this agency, but by all interested parties in 20 reducing harm caused by tobacco.</p> <p>21 So the IOM was, to me, also very correct 22 when it stated that the committee was particularly</p>

<p style="text-align: right;">Page 49</p> <p>1 wary. And this was, to me, one of the most 2 important statements of the report, even though 3 there's so much in there. They were wary of making 4 perishable recommendations that may lose relevance 5 as time passes and scientific methods and 6 technologies evolve.</p> <p>7 And that's where we are. We're in this new 8 era where we don't know where we're going and 9 what's going to happen. It is very clear to me 10 that by having these kinds of dialogues, we can 11 shape where we go. We can prevent problems of the 12 past. And we can see science evolve that is going 13 to develop new products that actually will do what 14 public health goals should be, and that is to 15 reduce disease and death caused by tobacco.</p> <p>16 I also believe -- and this has come up the 17 last couple of days -- that the FDA has a major 18 role in helping either to do the third-party 19 governance or providing the mechanisms to be able 20 to bring people together to do it. And that should 21 be explored on a continual basis. There should be 22 a follow-up meeting to this workshop where that</p>	<p style="text-align: right;">Page 51</p> <p>1 without sacrificing proper oversight.</p> <p>2 Public and private engagement of all 3 stakeholders for the discussion of science-related 4 issues in a neutral safe forum should be 5 encouraged, not discouraged.</p> <p>6 FDA should be commended for its leadership 7 role in advocating dialogue, and I strongly believe 8 that it should not retreat or back away from a more 9 transparent approach due to outside pressures.</p> <p>10 People want to participate; they participate. If 11 they don't want to participate; they don't 12 participate. But transparency and discussions, in 13 my view, are absolutely important.</p> <p>14 Justice Brandeis, famous saying again, 15 "Sunlight is the best disinfectant." And if we can 16 shine a light on the tobacco industry, and bring 17 them to the table to have dialogues and 18 discussions -- and, again, I'm not talking about 19 negotiations -- we can move this ball forward in a 20 much more significant manner.</p> <p>21 I've been proud to be a part of the 22 University of Virginia's Institute for</p>
<p style="text-align: right;">Page 50</p> <p>1 could be discussed on what that should look like, 2 and I would hope that that would happen.</p> <p>3 Just a few comments that I think need to be 4 incorporated, that any oversight must be of the 5 highest ethical standards. There must be 6 transparency -- you've heard transparency mentioned 7 over and over -- across the board. And every 8 effort should be made to minimize conflicts of 9 interest and interference. The development of 10 fair, consistent and uniform regulation and 11 standards that are applied to all entities seeking 12 approval of MRTP is essential. And there must be 13 continued open lines of communication. And as I 14 said before, the IOM correctly noted that some 15 flexibility is going to be needed to deal with 16 evolving technologies and scientific methods.</p> <p>17 Manufacturers, researchers, research 18 institutions and others should be a part of the 19 process by and through which the standards are 20 developed. And I think excessive regulatory and 21 even scientific bureaucracies that impede progress 22 in moving things forward should be avoided but</p>	<p style="text-align: right;">Page 52</p> <p>1 Environmental Negotiations that has held a series 2 of dialogues on tobacco-related issues. The first 3 ones they did were in the '90s and brought public 4 health and growers together. They have a track 5 record of success. They have started some new 6 dialogues, and I commend them for doing that. The 7 focus is on harm reduction issues, not on trying to 8 placate the industry or do anything like that, but 9 rather looking at the need for new policies related 10 to tobacco, nicotine and alternative harm reduction 11 strategies.</p> <p>12 They produced a set of core principles in 13 2011 on issues related to corporate funding for 14 tobacco, nicotine and alternative harm reduction, 15 which could help guide and stimulate further 16 discussions in the public and private sectors. I 17 will be submitting that on their behalf for the 18 record, but I'd like to sort of highlight a couple 19 of the things that were mentioned.</p> <p>20 Recognize and accepted, that it should be a 21 shared goal of all parties to reduce disease and 22 death caused by the use of tobacco; that science</p>

<p style="text-align: right;">Page 53</p> <p>1 should be used to assist the regulatory body in 2 setting the standards on how a spectrum of low risk 3 products should be labeled, sold and marketed. 4 That an independent third-party regulatory 5 authority such as the FDA is essential for 6 overseeing and setting fair, workable and effective 7 regulations designed to achieve goals that were 8 outlined in that first bullet that I mentioned 9 about a shared common objective. 10 That academic research institutions have in 11 place and promote publicly available conflict of 12 interest policies that prevent or limit the funder, 13 the research institution, the researcher from 14 misusing or distorting the purposes of the research 15 for which the funds have been allocated. Such 16 research should -- and this was a very important 17 component of this -- have a public health 18 objective. So it wasn't just general research that 19 went nowhere. It had to have public health goals. 20 That consideration should be given to the 21 development of models that can be used by research 22 institutions to establish the necessary safeguards</p>	<p style="text-align: right;">Page 55</p> <p>1 it's important, I think, to be able to look at that 2 from the broader perspective and start working with 3 USDA and others on those issues. 4 I wanted to leave you with a quote that was 5 made by former Commissioner David Kessler about 6 15 years ago at the conference that was sponsored 7 by FDLI and Georgetown University. And he said, "I 8 hope that someday the industry scientists would be 9 able to talk in a public forum about what they have 10 known and what they have learned about nicotine 11 administration over the years." 12 Well, I think we're there. We're at the 13 beginning of that process. I encourage all the 14 various interested parties and stakeholders to get 15 themselves involved, be transparent. Industry 16 should be opening its doors and inviting 17 researchers to come and inspect the research 18 facilities and their agendas, not have a 19 closed-door policy. 20 So there's a lot to be done, and I commend 21 the agency for holding this meeting today and look 22 forward to future meetings. Thank you.</p>
<p style="text-align: right;">Page 54</p> <p>1 that will ensure the highest integrity of the 2 research being conducted. 3 I also wanted to mention as I listened 4 yesterday about -- someone had said there was 5 limitations on the number of universities and 6 academic institutions receiving funding from the 7 tobacco industry. There's probably more than were 8 mentioned yesterday, but I also want -- Dr. Ashley 9 will know that I'm going to raise an agricultural 10 issue because there is a tremendous amount of 11 research going on in land grant colleges and also 12 other universities looking at the tobacco leaf. 13 My view is, is that the tobacco leaf is 14 going to play a very important role in the 15 development of modified-risk tobacco products, 16 particularly the noncombustibles, because that is 17 where you can remove the nitrosamines, reduce the 18 heavy metals, and do other things to the tobacco 19 that could actually have a very important impact, 20 public health impact, on users of those products. 21 So I don't want them to left out. I know 22 you don't have jurisdiction over that area, but</p>	<p style="text-align: right;">Page 56</p> <p>1 (Applause.) 2 MS. DILLEY: Similar to yesterday with the 3 panelists, we'll take a couple of questions. 4 Can you introduce yourself and wait for a 5 microphone? Again, we have people online, so. 6 MR. ROSE: Jed Rose. Thank you, Scott, for 7 that characteristically reasonable and balanced 8 summary. I was wondering if you see an 9 analogy -- you talk about the new era, and there's 10 been off and on discussion of history, one speaker 11 pointing out that often the tobacco control 12 community, some members of the tobacco control 13 community, have rehashed over and over the ancient 14 history, and history is continuing to evolve. 15 But do you see an analogy -- I remember 16 learning in high school that when the Revolutionary 17 War was fought with Great Britain that early on it 18 was very helpful to have very strident rebellious 19 activists like Patrick Henry, but then once the war 20 was won, it took the likes of Benjamin Franklin and 21 George Washington and so forth to craft the 22 Constitution and actually make progress with the</p>

<p style="text-align: right;">Page 57</p> <p>1 new society and getting work done.</p> <p>2 Do you see an analogy now that we are</p> <p>3 entering a new era where really constructive</p> <p>4 collaboration has to be the mantra?</p> <p>5 MR. BALLIN: I do, and I think our history</p> <p>6 is full of examples like that. I mean, you can</p> <p>7 look at the wars with Germany over the years. Do</p> <p>8 we still treat Germany as an enemy after having two</p> <p>9 miserable wars with them and the Japanese and</p> <p>10 everything else? Soviet Union, another example. I</p> <p>11 mean, there are tons of them out there, of examples</p> <p>12 where something happens that changes the debates</p> <p>13 and discussion, and I think that's what's happened</p> <p>14 here.</p> <p>15 It's hard to let go. I'm part of all of</p> <p>16 that era, that beating up on the industry, and I</p> <p>17 still will; I will continue to do that. But I also</p> <p>18 see an avenue here where instead of fighting the</p> <p>19 war and just lobbing bricks over the wall at each</p> <p>20 other, I think that by having meetings like this</p> <p>21 that are controlled, where people don't dominate</p> <p>22 it, one segment versus another, that we can</p>	<p style="text-align: right;">Page 59</p> <p>1 that mean concretely, what does that look like,</p> <p>2 transparency and independence.</p> <p>3 David.</p> <p>4 DR. ASHLEY: David Ashley, FDA. Scott, I</p> <p>5 was just very interested in one real small aspect</p> <p>6 of your slide. I wonder if you could help clarify</p> <p>7 it.</p> <p>8 You talk about the process needs to be</p> <p>9 consistent and flexible. And I find that very</p> <p>10 interesting. I'm just wondering if you've got some</p> <p>11 good examples of a system that's consistent and</p> <p>12 flexible.</p> <p>13 MR. BALLIN: I think that, for me, setting</p> <p>14 out broad principles that show consistency of a</p> <p>15 policy development but being able to be flexible if</p> <p>16 something changes. My own experience is that I</p> <p>17 could say that we'll carve everything in stone, and</p> <p>18 we won't deviate from it. That's consistent, but</p> <p>19 it's also unflexible because if I set out 10</p> <p>20 standards or 10 recommendations and say, this is</p> <p>21 what we think we need to achieve, there's got to be</p> <p>22 some flexibility about working within that system.</p>
<p style="text-align: right;">Page 58</p> <p>1 actually have some discussions to move it forward.</p> <p>2 It may be only a few things that move</p> <p>3 forward. There may not be much agreement on some</p> <p>4 stuff. But I have learned by my own experiences</p> <p>5 with working with the growers and working through</p> <p>6 this kind of a process that you don't know what to</p> <p>7 expect until you've actually sat down face-to-face</p> <p>8 with people in a safe environment and started some</p> <p>9 sort of a dialogue.</p> <p>10 MS. DILLEY: Are there any other questions?</p> <p>11 I think, too, that some of the discussion is</p> <p>12 focused on what are the criteria. I mean, there's</p> <p>13 part of the history, but there's also what are the</p> <p>14 criteria to get us to credible research. And there</p> <p>15 was a lot of discussion yesterday about</p> <p>16 independence and transparency, so what does that</p> <p>17 look like in going forward.</p> <p>18 Because I think your point, Jed, to some</p> <p>19 degree is so how do we move from where we are to</p> <p>20 where we need to go. And I think there was a lot</p> <p>21 of discussion of that yesterday, and hopefully</p> <p>22 we'll continue that today, focusing on what does</p>	<p style="text-align: right;">Page 60</p> <p>1 Does that answer your question?</p> <p>2 MS. DILLEY: You're looking for a specific</p> <p>3 example --</p> <p>4 DR. ASHLEY: Yes, that sounds -- I</p> <p>5 understand the principles and everything. The</p> <p>6 problem gets to be when you actually have to make</p> <p>7 regulatory decisions based on that, and I'm very</p> <p>8 interested in whether the industry wants us to be</p> <p>9 consistent or flexible. The word I've gotten is we</p> <p>10 need to be consistent, and then other times</p> <p>11 depending on the situation, they want you to be</p> <p>12 flexible. And so it's always an interpretation.</p> <p>13 It's just not an easy balance to achieve,</p> <p>14 particularly in a regulatory agency.</p> <p>15 MR. BALLIN: Yes, I agree with you a hundred</p> <p>16 percent. And I think that that's why these kinds</p> <p>17 of meetings are actually very important, because</p> <p>18 you can actually develop some consistency about</p> <p>19 where you need to go, some sort of direction that</p> <p>20 everybody might agree to. But then that roadmap is</p> <p>21 going to change as things change, and that's -- it</p> <p>22 happens in life all the time.</p>

<p style="text-align: right;">Page 61</p> <p>1 It's just not in a regulatory agency, but 2 things happen in our lives that we don't predict, 3 that we cannot control, even though our best 4 interests are to have some consistency in what we 5 want to achieve. I mean, I think we all make 6 decisions every single day that we wanted to do 7 something, and something got in the way and we had 8 to change the direction. 9 I think that the regulatory agency has to be 10 flexible enough, and I think that's what the IOM 11 suggested in a couple places in there, that we 12 can't put these recommendations in stone because 13 they're perishable, and we must be wary because of 14 the evolving science and technology. And I think 15 the FDA needs to take the same type of approach, 16 even though it wants some consistency and direction 17 about where it needs to head. 18 MS. DILLEY: One more question, and then we 19 need to move on. 20 MR. DELMAN: Hi, Scott. I really enjoyed 21 your comments this morning, as I generally do. 22 Farrell Delman from TMA.</p>	<p style="text-align: right;">Page 63</p> <p>1 is more acceptable by a broader spectrum of people. 2 As I said, the thing that I learned in 3 talking with farmers is there is so much 4 misinterpretation of people's views, and until you 5 have them in the same room, and you ask them a 6 question, and you have a dialogue about it or 7 discussion and get clarification, all you're doing 8 is polarizing the process. And I don't think we 9 are at a point here where we want to polarize 10 process anymore because we're in a regulatory 11 environment, and we've got a lot of different 12 stakeholders, and we've got different products 13 being developed by a broader spectrum of people, so 14 we need to think differently. 15 MS. DILLEY: Thanks, Scott, and you'll be 16 able to come back up at the end of this panel and 17 provide some more responses from our Q&A. 18 We need to move to our next presenter who's 19 Donald Graff, who's a clinical research scientist 20 with Celerion. 21 Presentation – Donald Graff 22 DR. GRAFF: So I think I'm going to switch</p>
<p style="text-align: right;">Page 62</p> <p>1 I'm wondering if you had a chance to listen 2 in on yesterday's conversation where we discussed 3 quite a bit the IOM recommendations, and there was 4 a number of comments associated with Recommendation 5 Number 10, particularly, and concern among some of 6 the people here that preapproval of third parties 7 is a recommendation they could not support. And I 8 think the sense was that such preapproval of third 9 parties might lend itself to violating in some 10 sense the overall objectives of the independence of 11 third-party governance. 12 I guess I'm wondering if you've got any 13 thoughts at all on Recommendation Number 10 and the 14 conversation that we had yesterday. 15 MR. BALLIN: You know, Farrell, I don't 16 because, as I said, I'm not a scientist or a 17 researcher, and there are a lot of issues that go 18 with that. But what I would say is that's a 19 perfect topic for further discussion here at FDA 20 and outside of FDA, because if people were to sit 21 down and maybe work through some of these things 22 and issues, maybe something could be developed that</p>	<p style="text-align: right;">Page 64</p> <p>1 directions here pretty significantly. Yesterday, 2 we also had a presenter who's working from the 3 trenches, and I sort of see myself in that regard 4 as well. So as the sign says, my name is Don 5 Graff, and as a clinical research scientist at 6 Celerion, part of my job is to design studies and 7 write protocols as well as analyze and interpret 8 data and write clinical study reports for our 9 tobacco sponsors. 10 For those of you who might be unaware, 11 Celerion is a contract research organization, or 12 CRO, that focuses primarily on conducting early 13 phase clinical research studies for pharmaceutical 14 companies. However, over the last 12 years and 15 including under our previous name of MDS Pharma 16 Services, we have performed clinical conduct, 17 analyzed data or analyzed biological samples for 18 more than 50 studies for tobacco companies. 19 So it's with that experience that I 20 understand that the development of modified-risk 21 tobacco products is going to be an effort that will 22 benefit from the expertise of individuals in areas</p>

<p style="text-align: right;">Page 65</p> <p>1 such as academia, public health, and government 2 and, of course, the tobacco industry itself. 3 So I'd like to start off with just 4 highlighting a couple of benefits that I think that 5 CROs could bring to the table in this regard. On a 6 high level, areas of essential expertise that I 7 think the CRO industry does bring to the table 8 include working with good clinical and laboratory 9 practices and regulatory submissions. And it's 10 because that we live in this GxP and regulatory 11 environment day by day, in my opinion, there's no 12 better partner that a tobacco company could have 13 than a CRO when it comes to performing this work to 14 meet ethical, scientific, and regulatory demands 15 that are going to be necessary. 16 So the advantages then of working with a 17 third party adept in best practices and industry 18 standards is getting better, cleaner data to the 19 FDA, which I'm sure that they appreciate, or we've 20 come to know that they appreciate clean data, more 21 quickly and at a lower cost. And similar to our 22 pharmaceutical work, there are going to be</p>	<p style="text-align: right;">Page 67</p> <p>1 are going to be needed to bring new products to 2 market in a timely manner. 3 So on the next few slides here, I touch on 4 some of the high level challenges that we face in 5 general when it comes to conducting tobacco 6 studies. As you can imagine, there are a number of 7 operational and logistical challenges as well with 8 any clinical trial or a set of clinical trials, but 9 I'm not going to go into a lot of specifics in 10 these remarks. 11 The first of the challenges that I would 12 like to bring out, in my opinion, is the most 13 significant challenge that we have, is how do we 14 meet the FDA's requirements and expectations. I do 15 commend the FDA for the guidance that they have 16 been able to put into place so far, but from an 17 operational standpoint, these guidances primarily 18 provide high level direction. And from our 19 perspective, there are a number of specific details 20 that are yet to be determined. 21 Looking to the pharma industry, for example, 22 when it comes to early phase research, I can find a</p>
<p style="text-align: right;">Page 66</p> <p>1 successful products and unsuccessful products. 2 So the primary concern that I have is only 3 that we provide a high quality deliverable at the 4 end of the project or program, and, of course, we 5 always hope for the best outcomes for both our 6 pharmaceutical and tobacco sponsors. But we often 7 have to remember that success can also be defined 8 as getting a failing or harmful product out of the 9 development chain as soon as possible. 10 So at the project level then, experience and 11 expertise that can be found in a CRO can 12 specifically help with the public perception issue 13 that exists and help to reduce the potential for 14 bias in study design, statistical analysis, and 15 data interpretation of a tobacco trial, just as it 16 can in our relationship with the pharmaceutical 17 industry. 18 Because we are looking at new product 19 applications as the end product here, in my 20 opinion, no other group has the capacity to conduct 21 the number of trials, recruit the number of 22 subjects, and analyze the mountains of data that</p>	<p style="text-align: right;">Page 68</p> <p>1 guidance document on just about every study that I 2 would need in order to move a drug through the 3 development process. So my hope is that the FDA 4 follows this model and expands upon the information 5 that is in the current guidance and perhaps 6 provides some sort of formal framework to bring a 7 product to market. 8 So with regard to what we can take from the 9 guidance documents that are currently available, in 10 my opinion, the exposure studies and most of the 11 health risk evaluations for tobacco consumers that 12 are going to be required are relatively 13 straightforward. But it's the requirements for the 14 evaluations of non-consumers' perception-type 15 studies and post-marketing studies, especially, 16 where companies in our industry might need to call 17 upon experts in other areas for their expertise. 18 For example, evaluations that include 19 adolescents and other vulnerable populations that 20 were mentioned yesterday, according to the 21 regulation, these evaluations need to take place in 22 order to get a product approved. So somebody's got</p>

<p style="text-align: right;">Page 69</p> <p>1 to carry them out, but who? If we are to be 2 involved, we in the CRO industry are going to 3 either have to adapt our services or call on 4 experts in academia or public health to help with 5 items such as this.</p> <p>6 Next, statistically, what is going to be the 7 burden of proof when it comes to demonstrating 8 success or failure, and how do we define 9 appropriate for the benefit of the public health? 10 Will a definition of clinical significance need to 11 be determined for various evaluations, or will a 12 simple statistically significant finding be 13 sufficient?</p> <p>14 With regard to how the introduction of a new 15 product into the market will affect things like 16 cessation or initiation, will any decrease in the 17 cessation rate or increase in the initiation rate 18 be acceptable, even if overall exposure to harmful 19 or potentially harmful constituents are reduced? 20 And when it comes to evaluating these HPHCs, are 21 any more critical than others? So what if some 22 constituents go up slightly and others go down?</p>	<p style="text-align: right;">Page 71</p> <p>1 research exemptions for combustible product use 2 indoors. And as these cigarettes become more and 3 more popular, more and more states are also 4 including them in their indoor smoking bans as 5 well.</p> <p>6 So based on my very non-expert 7 interpretation of the state laws in all 50 8 states -- I'm a scientist and not even close to 9 having the legalese when it comes to evaluating or 10 interpreting laws. But according to what I've 11 seen, there's only 14 states where it appears to be 12 clear that we can conduct in clinic evaluations of 13 combustible products.</p> <p>14 This, of course, makes it much more 15 challenging to meet the regulatory requirements, as 16 it is clear that even for new noncombustible 17 products, evaluations will need to include 18 comparisons to conventional combustible products as 19 well.</p> <p>20 So when we do identify states where the work 21 can be performed, we need to find facilities that 22 are equipped to actually do the work, as special</p>
<p style="text-align: right;">Page 70</p> <p>1 These are just a few of the more basic 2 questions that we have had when reading the 3 guidances, and it would be very helpful if these 4 kinds of questions were considered in future 5 guidance documents so that we can design studies 6 appropriately.</p> <p>7 Then to the last bullet here, how do we 8 balance the benefit to individuals to that of the 9 population of the whole? Certainly, public health 10 should be considered and the burden of proof should 11 be set very high, no doubt, but not so high that 12 it's impossible to approve reduced risk products 13 that could replace more harmful products, thereby 14 eliminating the benefit to consumers who wish to 15 use them.</p> <p>16 So next, there's some site selection and 17 challenges in facilities' needs that need to be 18 dealt with when it comes to conducting tobacco 19 studies. As we've been evaluating our need to 20 develop clinical partners for this work, we've 21 found that few states have clear language within 22 their tobacco regulations that provide clinical</p>	<p style="text-align: right;">Page 72</p> <p>1 processes, procedures and SOPs must be put into 2 place to carry out the activities are required for 3 evaluating tobacco products. For example, does the 4 facility have an adequate ventilation system that 5 isolates air flow from rooms where smoking occurs 6 so that it is not redistributed to other sections 7 of the facility?</p> <p>8 To go along with that, there are staffing 9 considerations and investigator qualifications that 10 also need to be considered. At Celerion, for 11 example, we do not require our nonsmoking staff to 12 participate in clinical conduct events where 13 smoking takes place. And in addition, due to the 14 very low limit of quantitation for nicotine that we 15 have in our bioanalytical lab, we also can't allow 16 staff members who smoke or use tobacco products to 17 perform some processing steps so that we can avoid 18 contamination of the samples. So appropriately 19 staffing these studies can also be a challenge.</p> <p>20 So next are some ethical considerations. 21 Obviously, there's more ethical considerations than 22 what we can discuss here in the time that I have,</p>

<p style="text-align: right;">Page 73</p> <p>1 but these are some of the items that we're looking 2 at currently.</p> <p>3 An important consideration here is how do we 4 fully understand new products without encouraging 5 or increasing their use. Obviously, we don't want 6 to introduce a product to someone who otherwise may 7 not have considered trying the product, such as 8 adolescents and other vulnerable populations.</p> <p>9 Also, at the project level, clinical trials 10 require subject compensation, and sometimes study 11 products are provided to subjects free of charge 12 during the study. So this can be problematic, as 13 it may be perceived that subjects are being coaxed 14 into trying something new. Hence, we are very 15 careful when we create the inclusion and exclusion 16 criteria for these studies and determine 17 compensation rates in order to minimize any ethical 18 issues and operational problems that might arise in 19 the face of this free product effect.</p> <p>20 This next bullet might also be considered an 21 ethical matter for individuals called on to do the 22 work, and that is, as a healthcare professional,</p>	<p style="text-align: right;">Page 75</p> <p>1 every study that we work on with the highest 2 integrity.</p> <p>3 So we might find ourselves, for example, 4 educating the IRB or ethics committee, facilities, 5 vendors, other subject matter experts that we might 6 call on as the needs arise, especially if they have 7 not been involved in such studies in the past.</p> <p>8 Lastly, even the Pharma-CRO model has its 9 limitations and drawbacks when it comes to being an 10 all-inclusive partner in this. While there are 11 many similarities to our pharma work, there are 12 numerous operational and logistical details that 13 need to be taken into account with this kind of 14 research. So significant pharma experience does 15 not necessarily guarantee success in this market 16 space.</p> <p>17 Also, because of some of the special 18 requirements of this work, there may be gaps in the 19 current expertise and facilities available within 20 CROs currently that need to be filled either 21 internally or by partnering with external subject 22 matter experts. So not all CROs could provide</p>
<p style="text-align: right;">Page 74</p> <p>1 how do you justify working on tobacco products? 2 For me as a former and sometimes current practicing 3 pharmacist, it's not a question that I struggle 4 with anymore, especially when I keep in mind that 5 the goal here is to reduce tobacco-related 6 morbidity and mortality by bringing less toxic 7 products to market. If we're able to reduce from 8 the 440,000 deaths that are attributed to smoking 9 each year in the U.S. by significantly reducing 10 exposure to toxicants, then we have achieved that 11 goal, in my opinion.</p> <p>12 Also, there's a significant need for 13 education regarding how tobacco product research 14 and healthcare align. We're all familiar with the 15 burden that tobacco has put on healthcare as well 16 as the benefits, or the potential benefits, that 17 might come from modified-risk tobacco products. 18 But in order to make this work rather than dwelling 19 on the past, we need to focus more on what we can 20 do to conduct this research to the highest ethical 21 and scientific standards going forward. And at 22 Celerion, we feel that we do this with each and</p>	<p style="text-align: right;">Page 76</p> <p>1 comprehensive program oversight on their own. 2 However, I firmly believe that if a CRO wants to 3 contend in this space, that it will find a way to 4 fill those gaps.</p> <p>5 Finally, and I think very importantly, 6 considering the overall topic of the workshop here 7 today and yesterday, bias and preconception may be 8 minimized with a model that closely follows the 9 Pharma-CRO model, but no model or governance 10 structure will ever be able to completely eliminate 11 them. So just as there may have been indiscretions 12 in the development of pharmaceutical products in 13 the past, we also run the risk in this area of 14 research. So all stakeholders must remain vigilant 15 to keep this work to the highest ethical and 16 scientific standards.</p> <p>17 Finally, just a couple of concluding 18 thoughts here. I'd like to note that we must not 19 forget that the objective of MRTP approval is to 20 provide safer products for consumers who wish to 21 take part in a legal activity and that the 22 Pharma-CRO model would provide an excellent</p>

<p style="text-align: right;">Page 77</p> <p>1 starting point to provide independent third-party 2 oversight of tobacco-related research. 3 Thank you. 4 (Applause.) 5 MS. DILLEY: We have time for one or two 6 questions before we take a break, questions or 7 clarification. 8 MS. GAGOSIAN: Hi. Stacey Gagosian with 9 Legacy. I'm not familiar with the pharmaceutical 10 approval process. 11 Do you-all contract directly with the 12 sponsors, or do you go through FDA? 13 DR. GRAFF: So almost invariably, we 14 contract directly with pharmaceutical companies or 15 biotech companies. On occasion, especially when we 16 work with some of the small biotech companies, we 17 might contract with a third party who's sort of 18 overseeing their development. But, typically, we 19 don't directly work with the FDA. I mean, we 20 obviously have a lot of interaction with the FDA, 21 but not from a contractual standpoint. 22 DR. BACKINGER: Good morning. Cathy</p>	<p style="text-align: right;">Page 79</p> <p>1 subjects to be at least 19 years of age in Nebraska 2 for the studies that are run there, and usually, 3 they're even a little bit higher because of some 4 smoking history requirements that are also 5 considered in some of those studies. 6 DR. BACKINGER: And just looking at your 7 concluding thoughts, your first bullet about 8 consumers who wish to take part in legal activity, 9 research over the past many decades show that most 10 adults -- 87, I think, percent of adults who smoke 11 started smoking before they were 18. And the 12 statute dictates that we need -- that a sponsor of 13 an MRTPA need to take into account both users and 14 non-users, including vulnerable populations such as 15 youth. So it's an important consideration. 16 DR. GRAFF: Absolutely. And I can tell you 17 that, again, as we evaluate external clinics that 18 we might work with to conduct some of this 19 research, I can tell you that in some cases, those 20 independent clinics have done smoking cessation 21 work and evaluations with adolescents. So when I 22 say specifically my company has not, it doesn't</p>
<p style="text-align: right;">Page 78</p> <p>1 Backinger, Center for Tobacco Products, FDA. You 2 mentioned in your slide on ethical considerations 3 around youth -- and obviously, of course, there are 4 ethical considerations. But through NIH and other 5 federal agencies, there's been research conducted 6 with youth around perceptions of tobacco products, 7 following kids over time to see if they initiate or 8 start. 9 I'm wondering, does your company do work 10 with youth from your other work, or is that -- what 11 is your policy in that regard? 12 DR. GRAFF: So historically, even with 13 pharmaceutical products, we haven't done a lot of 14 work with children, adolescents, in that regard. 15 It had a lot to do with the IRB that we used to 16 have as MDS Pharma Services. They just weren't 17 comfortable reviewing, for the most part, work with 18 children. So we've sort of avoided that. In that 19 tobacco area, no, we have not done any work with 20 adolescents or youth of any kind. 21 Typically, when we're designing our studies, 22 the inclusion and exclusion criteria require</p>	<p style="text-align: right;">Page 80</p> <p>1 mean that some of the other clinical facilities 2 that we have had talks with don't do that work. 3 And, of course, it is very important. 4 MS. DILLEY: Okay. I would like to take a 5 break now and come back at 10:15. Donald will have 6 a chance to respond to additional Q&A when we get 7 to that point in the day. So we'll start right 8 back up at 10:15. 9 (Whereupon, a recess was taken.) 10 MS. DILLEY: So we wanted to keep pretty 11 much on time because we do have a series of five 12 speakers for this next stretch, and then we'll move 13 into Q&A with all the panel members, so that will 14 be seven people. 15 Next up is Lars-Erik Rutqvist, who's the 16 senior vice president of scientific affairs at 17 Swedish Match. 18 Presentation -- Lars-Erik Rutqvist 19 DR. RUTQVIST: Thank you, and good morning. 20 I'd like to start this presentation by noting that 21 research governance is not a new issue, nor just a 22 tobacco issue. There are several product areas out</p>

<p style="text-align: right;">Page 81</p> <p>1 there that have governance structures implemented 2 more or less successful. And although tobacco is 3 different, not least because of the public health 4 provision and the Tobacco Control Act, and 5 therefore requires extra scrutiny, it is reasonable 6 that the establishment of an infrastructure for 7 tobacco builds on the experiences that FDA has from 8 other fields. And so it's natural that the Center 9 for Tobacco Products provides leadership in this 10 development.</p> <p>11 With that said, it's equally important that 12 industry and other stakeholders are open minded and 13 are willing to change and contribute thoughts to 14 the process because, otherwise, if you're not 15 interested in a dialogue around these issues, you 16 run the risk of becoming irrelevant to the process.</p> <p>17 The chapter on governance in the IOM report 18 was not surprising. Now, whether you agree with 19 the conclusions or not in the chapter on 20 governance, I think you have to accept that it 21 accurately reflects how the tobacco industry is 22 perceived. But I don't think that considerations</p>	<p style="text-align: right;">Page 83</p> <p>1 hard copies of that paper outside this conference 2 room, and if you can't find them, please approach 3 Jim during the break. I know he has some hard 4 copies, also.</p> <p>5 I'd also like to acknowledge the initiative 6 taken by a group of tobacco researchers a couple of 7 years ago. They met to explore innovative funding 8 models for tobacco research, and we heard Joanna 9 Cohen elaborate on this initiative yesterday.</p> <p>10 In order to be realistic, I think we have to 11 accept that it will take time to establish a 12 comprehensive governance infrastructure for 13 tobacco. But research on MRTPs cannot wait. Since 14 the Tobacco Control was passed in 2009, there's 15 been a significant increase of research articles on 16 this subject. And I don't think that this momentum 17 should be slowed by these deliberations about how 18 the research governance infrastructure should look 19 like. In this context, it's important for industry 20 to be aware of this issue and contribute thoughts 21 as to how the process can be approved.</p> <p>22 Yesterday, we heard about models for how</p>
<p style="text-align: right;">Page 82</p> <p>1 related to the troubled past of the U.S. tobacco 2 industry should make us lose sight of what's 3 important today in this new era of the Tobacco 4 Control Act. And I'd like to quote from the report 5 that, "Establishing the tobacco industry as a 6 legitimate participant in tobacco research is an 7 important consideration in the overall goal of 8 producing evidence on the effect of modified-risk 9 tobacco products."</p> <p>10 I only wish the IOM committee had offered a 11 more defined path forward to the establishment of a 12 comprehensive research governance structure for 13 tobacco, but that was perhaps beyond the scope of 14 the committee's charge. And so I think it might be 15 a good idea to appoint a new committee to provide 16 the necessary follow-up.</p> <p>17 I think we should also be aware that there 18 are governance models out there to consider, and my 19 Swedish Match colleague Jim Solyst recently wrote 20 an article for the FDLI journal named, Will Public 21 Private Research Partnerships Improve Research 22 Funding and Application? And I know there are some</p>	<p style="text-align: right;">Page 84</p> <p>1 third parties can assume key functions of research 2 governance such as funding, setting research 3 priorities, and actually doing the actual research 4 themselves. But companies have a -- the Tobacco 5 Act requires product-specific research when it 6 comes to modified-risk products, and companies 7 because of their product stewardship commitment 8 should also do research. And I think there are 9 examples of the types of research that it would be 10 very difficult for third parties to assume key 11 functions of governance. And I think a good 12 example of that type of research is the development 13 of the GothiaTek standard for snus products. That 14 standard was developed by Swedish Match. It 15 originated as a collaboration between toxicologists 16 at the Swedish Food Authority and the company, but 17 the continued research required to develop the 18 standard was done within the company. And it was 19 based on an intimate knowledge of all parts of the 20 manufacturing process. And I don't really see how 21 a third party really could have contributed to that 22 research effort. So I think product-specific</p>

<p style="text-align: right;">Page 85</p> <p>1 research should be both a corporate obligation, but 2 with the Section 911, it could also be a 3 competitive necessity. 4 The MRTP process requires product-specific 5 evidence, and therefore, it's in the best interest 6 of companies and public health that this research 7 proceeds in a timely manner. And I think the 8 conclusion that I'm getting at is that before a 9 comprehensive governance model has been codified or 10 mandated, companies must institute their own 11 research governance. 12 As an example, let me mention the clinical 13 trials with snus that Swedish Match has sponsored 14 in recent years, and these studies were initiated 15 well before the Tobacco Control Act was passed. I 16 won't go through all of these bullet points, but 17 let me just say that even though there was no 18 Tobacco Control Act, we were aware that credibility 19 of the evidence was a key issue. And in order to 20 ensure credibility, we thought the best idea was to 21 institute proper governance of the trial, and we 22 more or less emulated the pharma model for</p>	<p style="text-align: right;">Page 87</p> <p>1 such as this had its challenges, and I won't go 2 through all of them. But just let me mention that 3 there are some IRBs or ethical committees out there 4 who consider all studies involving tobacco uses as 5 inherently unethical unless they aim at total 6 tobacco abstention. And, of course, that type of 7 position is not consistent with the research on 8 modified-risk tobacco products, and, unfortunately, 9 we lost a number of centers because of this 10 problem. 11 Also, recruitment of CROs can be a problem. 12 I found that some CROs in this country have a 13 policy of not working with tobacco companies, 14 policies that sometimes are explicit, and sometimes 15 you find out after a while that they are not 16 comfortable working with a tobacco company or with 17 a tobacco product. 18 Also, for CROs that are willing to work with 19 a tobacco company, there are a lot of challenges, 20 and I think the gentleman from Celerion very 21 adequately presented some of the problems for a CRO 22 to work with a tobacco company and with tobacco</p>
<p style="text-align: right;">Page 86</p> <p>1 governance but added a few extra features. 2 Let me just highlight where we involved 3 third parties. For instance, the protocols were 4 developed not by us, which is sometimes the case in 5 pharma trials, but they were a collaboration 6 between the individual research teams that did the 7 research and Swedish Match. Also, we used contract 8 research organizations to be responsible for all 9 data handling, data monitoring, and statistical 10 analyses according to prespecified statistical 11 analyses plans. 12 We registered the trials in public databases 13 such as clinicaltrials.gov. And finally, already 14 at the outset, we made a commitment to publish the 15 results of the trials irrespective of the outcome. 16 We also made a commitment to make individual 17 patient data from the studies available for 18 systematic reviews and meta-analysis. I'm sure 19 you're aware that this is something that pharma 20 companies sometimes have been criticized for not 21 doing. 22 Now, implementing a governance structure</p>	<p style="text-align: right;">Page 88</p> <p>1 products. 2 The third bullet point is not relevant for 3 studies conducted here in the United States, but 4 internationally, it can be challenging to perform 5 studies with a tobacco product where there's no 6 traditional use of the product category. Just 7 getting it over the border can be a difficulty. 8 In some countries, there are regulations 9 that state that all clinical trials must be 10 approved by the Medical Products Agency. And to 11 have such an agency approve a trial with a tobacco 12 product can be quite challenging. 13 As transparency and external oversight are 14 central components of any successful governance 15 structure, Swedish Match has decided to take a 16 further step when it comes to research related to 17 MRTP products. And so I'm delighted to be able to 18 make it public today that Swedish Match has 19 initiated an external independent advisory panel on 20 matters related to research and analysis for 21 modified-risk tobacco products. 22 The founding member of the panel is</p>

<p style="text-align: right;">Page 89</p> <p>1 Professor Karl Fagerstrom. It was natural for us 2 to turn to him because we worked previously on the 3 clinical trials, but the other members of the panel 4 are U.S. based and represent the broad range of 5 relevant science areas; for instance, risk 6 communication, toxicology, research ethics and, of 7 course, tobacco research. 8 Now, I'd like to emphasize that I cannot 9 speak on behalf of the panel because it is an 10 independent body that will develop its own mission 11 statement, and the members are free to raise any 12 relevant issue. But just let me mention that the 13 panel's deliberations will be guided by the public 14 health interest. There will be no contractual or 15 confidentiality agreements between the company and 16 the panel members. And I know that the panel would 17 like its activity to serve as a model for how a 18 tobacco company can interact with an external 19 science-based group. 20 The inaugural meeting was held just a few 21 weeks ago, so this is a completely new panel. It's 22 evolving. So what the eventual outcome will be of</p>	<p style="text-align: right;">Page 91</p> <p>1 MR. APELBERG: Ben Apelberg, Center for 2 Tobacco Products, FDA. 3 I just had a clarifying question for the 4 point you mentioned about the commitment to make 5 individual study data available. So does that 6 include sort of availability to independent 7 academic researchers who would want to analyze it 8 and publish a systematic review or analysis? And 9 if so, have you thought about a process for making 10 that available, and have you actually done that 11 yet? Or is this sort of talking about a principle 12 that you intend to put in place? 13 DR. RUTQVIST: Well, the answer to your 14 first question is yes. The trials have been 15 published. So far, we have received no requests 16 for making access to the data. We've also done a 17 systematic review and meta-analysis of the trials. 18 That paper was recently accepted for publication. 19 Perhaps that will stimulate the interest in the 20 trials and will sort of make people aware of the 21 fact that you can do that. And if we receive such 22 a request, we will definitely make the data</p>
<p style="text-align: right;">Page 90</p> <p>1 the panel's activities, obviously, is difficult or 2 even impossible to predict today. But, obviously, 3 we're all very excited to work on this initiative. 4 So, in conclusion, I think that 5 comprehensive tobacco research governance 6 infrastructure is badly needed, and the Section 911 7 of the Tobacco Control Act is a potentially 8 powerful tool to achieve this. I think that the 9 CTP should continue the types of dialogues that are 10 exemplified by this workshop, and I think also that 11 CTP should consider funding an IOM committee 12 charged with elaborating on the ideas in the 13 governance section of their recent report. 14 But we should also be aware that governance 15 is a long-term project, and in the meantime, 16 research must continue. And companies like Swedish 17 Match need to establish their own governance 18 provisions. 19 Thank you. 20 (Applause.) 21 MS. DILLEY: We can take a couple of 22 questions.</p>	<p style="text-align: right;">Page 92</p> <p>1 available. 2 MS. DILLEY: Other questions? 3 DR. HUSTEN: Corinne Husten, CTP. I just 4 had a question about the advisory panel that you're 5 setting up. 6 Will those meetings be like open public 7 meetings? 8 DR. RUTQVIST: That is something that the 9 panel would decide. I don't know. 10 MS. DILLEY: So they're structuring their 11 own governance? 12 DR. RUTQVIST: Yes. 13 MS. DILLEY: Matt? 14 MR. MYERS: Thank you. That was 15 interesting. 16 MS. DILLEY: Can you introduce yourself? 17 MR. MYERS: Sure. I'm Matt Myers with the 18 Campaign for Tobacco-Free Kids. 19 I've heard you and your colleagues speak 20 before and speak pretty glowingly about the 21 research done on the GothiaTek method, and you 22 highlighted that there as an example of a kind of</p>

<p style="text-align: right;">Page 93</p> <p>1 research a company should be doing; and heard you</p> <p>2 previously talk about the belief about the low</p> <p>3 level of disease risk of products that meet the</p> <p>4 GothiaTek standard with regard to that.</p> <p>5 So I guess my question is how that</p> <p>6 translates. Do your products in the United States</p> <p>7 meet the GothiaTek standard? And while your</p> <p>8 presentation focused on Section 911, if, in fact,</p> <p>9 GothiaTek standard was shown to be significantly</p> <p>10 less hazardous than even other smokeless tobacco</p> <p>11 products, would you support a Section 907 product</p> <p>12 standard so that everybody is protected by that?</p> <p>13 DR. RUTQVIST: You should know that the</p> <p>14 GothiaTek standard is a product standard for snus,</p> <p>15 and it's a comprehensive product standard that</p> <p>16 doesn't only include the maximum levels of certain</p> <p>17 selected toxic compounds. It's a standard for</p> <p>18 production technique, for qualified consumer</p> <p>19 information, which, obviously, we can only</p> <p>20 implement outside of the U.S. at the moment.</p> <p>21 MR. MYERS: But there's no technical reason</p> <p>22 why you couldn't in the United States.</p>	<p style="text-align: right;">Page 95</p> <p>1 standard. Am I right about that?</p> <p>2 DR. RUTQVIST: All snus products in Sweden</p> <p>3 and in the U.S. manufactured by Swedish Match meet</p> <p>4 the standard.</p> <p>5 MR. MYERS: But in Sweden, do you make any</p> <p>6 other smokeless tobacco products?</p> <p>7 DR. RUTQVIST: No.</p> <p>8 MR. MYERS: No. And so I guess my</p> <p>9 question -- in the literature I've read, you've all</p> <p>10 talked about one of the reasons for that is the</p> <p>11 government has set that as a standard because of</p> <p>12 health and safety concerns. And so I guess what</p> <p>13 I'm asking is, if it's good enough in Sweden, why</p> <p>14 don't we do it in the United States?</p> <p>15 DR. RUTQVIST: You should ask that question</p> <p>16 to the CTP, not to me.</p> <p>17 MR. MYERS: But what I'm asking you is with</p> <p>18 Swedish Match, would you at Swedish Match support</p> <p>19 not just a 911 exception but support that all</p> <p>20 smokeless tobacco products meet that standard?</p> <p>21 DR. RUTQVIST: Yes.</p> <p>22 MS. DILLEY: All right. Thank you very</p>
<p style="text-align: right;">Page 94</p> <p>1 DR. RUTQVIST: But all snus products sold by</p> <p>2 Swedish Match here in the U.S. adheres to the</p> <p>3 GothiaTek standard, but I'm sure you know that</p> <p>4 Swedish Match also manufactures American moist</p> <p>5 snuff products. And we worked over several years</p> <p>6 to make them comply with the maximum levels of</p> <p>7 these potentially toxic compounds that are covered</p> <p>8 by the standard, and we've come quite far with</p> <p>9 that.</p> <p>10 But because of manufacturing differences and</p> <p>11 the obvious product differences, there are a few of</p> <p>12 these compounds that we still don't meet the</p> <p>13 GothiaTek standard. But I think if the GothiaTek</p> <p>14 standard, which is at the moment a voluntary</p> <p>15 standard -- if it were accepted, I think it would</p> <p>16 be an enormous competitive advantage to have</p> <p>17 products comply with the standard. So I think you</p> <p>18 would see a development for many products towards</p> <p>19 that goal, if it were accepted.</p> <p>20 MR. MYERS: I'm confused. Just pure point</p> <p>21 of clarification. In Sweden, all products, all</p> <p>22 non-combusted products that you sell meet that</p>	<p style="text-align: right;">Page 96</p> <p>1 much. And people will have a chance to ask</p> <p>2 Lars-Erik more questions when we have the Q&A for</p> <p>3 the full panel.</p> <p>4 So next we have Michael Ogden who's senior</p> <p>5 director of regulatory oversight, RAI Service</p> <p>6 Companies, R.J. Reynolds Tobacco Company.</p> <p>7 Presentation - Michael Ogden</p> <p>8 DR. OGDEN: Thank you. Good morning, ladies</p> <p>9 and gentleman. Mike Ogden, RAI Services Company.</p> <p>10 I'm here on behalf of CTP-regulated tobacco</p> <p>11 operating companies under the RAI operating family.</p> <p>12 It includes R.J. Reynolds Tobacco Company, the</p> <p>13 American Snuff Company, and Santa Fe Natural</p> <p>14 Tobacco Company.</p> <p>15 Just a brief outline of my comments this</p> <p>16 morning. I'll start with a few key takeaways.</p> <p>17 Give you our view of the transformation that's</p> <p>18 going on in the U.S. tobacco industry. We believe</p> <p>19 that we are championing that effort. Talk briefly</p> <p>20 about some issues and opportunities with</p> <p>21 third-party governance. And for that conversation,</p> <p>22 I'll frame it in light of a couple of the IOM</p>

<p style="text-align: right;">Page 97</p> <p>1 recommendations. And then we'll talk about some 2 key conclusions. 3 One point I'd like to make clear -- and I 4 was in the audience yesterday, as many if not most 5 of you were as well, and there seemed to be a bit 6 of conflation of the different types of research 7 that might be -- that will be required under a 8 modified-risk tobacco product application. I don't 9 know if that was intentional or perhaps even 10 desirable, but basically as I sat and listened to 11 those comments and the discussions yesterday, it 12 was often unclear as to which piece of the research 13 one was speaking about. 14 I easily see three areas of research 15 relevant to modified-risk tobacco products. 16 There's the development of research tools that 17 could be used broadly across any potential 18 modified-risk tobacco product. There's also the 19 product-specific research that's required to 20 support an application, and then there's obviously 21 requirements for post-market surveillance, both in 22 development of tools and also the implementation of</p>	<p style="text-align: right;">Page 99</p> <p>1 ones and perhaps some new ones. But a key point 2 that we would like to bring forward is that in our 3 view, all stakeholders need to be appropriately 4 involved. And the tobacco company itself that is 5 sponsoring the modified-risk tobacco product 6 application is, in our view, a key stakeholder, and 7 they must then be involved. 8 So a quick view of transforming tobacco in 9 terms of RAI's operating companies, we're committed 10 to transforming the U.S. tobacco industry. We have 11 invested heavily in the potential to reduce the 12 harm associated with cigarettes, going back more 13 than 25 years, and that continues to this day with 14 some examples that will become clearer perhaps in a 15 moment. And we're committed to meeting society's 16 expectations for how a tobacco company should 17 operate. 18 Just to give you a brief view of the RAI 19 operating companies, you know, of course, perhaps 20 the largest company is the R.J. Reynolds Tobacco 21 Company that manufactures cigarettes and smokeless 22 tobacco products; the American Snuff Company, which</p>
<p style="text-align: right;">Page 98</p> <p>1 those research tools. 2 So I thought it was a useful comment to put 3 that in front of you, and then to say as a preamble 4 to my comments, the majority of what I will speak 5 about is that second research bucket. And that is 6 the product-specific research required to support a 7 modified-risk tobacco product application, but I 8 also will touch out to some of the others as well. 9 So key takeaways from our 10 perspective -- when I speak of the industry, I'll 11 speak, most importantly of course, of the RAI 12 tobacco operating companies. Industry already does 13 most of what IOM recommends. Some of the IOM 14 recommendations -- and I'll elaborate on those in a 15 moment -- appear to be unreasonable, unworkable, 16 and I'll point those out, as I said. 17 In our view, independent third-party 18 governance is not needed, but collaboration on 19 certain research areas could be useful in some 20 areas. Some types of research could resolve some 21 problematic issues. You've already heard about 22 some of those, and I will mention some of the same</p>	<p style="text-align: right;">Page 100</p> <p>1 we acquired nearly a decade ago that manufactures 2 traditional America moist products and other 3 smokeless products and the Santa Fe Natural Tobacco 4 Company. 5 But we've also recently acquired or 6 developed other operating companies. One is 7 Nicovum that operates in the nicotine replacement 8 therapy space. It is not CTP regulated, but it is 9 regulated by FDA's CDER. And we've recently in the 10 last couple of years begun developing work and 11 products and marketing in the e-cigarette category 12 under the R.J. Reynolds Vapor Company. And as 13 you've also heard yesterday and today, that's 14 certainly an emerging area of great interest to 15 tobacco companies, to other companies, and to the 16 consuming public. 17 So what's our view of tobacco regulation? 18 Tobacco products should be regulated in a manner 19 that's designed to achieve significant and 20 measurable harm reduction. It should obviously 21 enhance the information available to consumers and 22 encourage the development of tobacco and nicotine</p>

<p style="text-align: right;">Page 101</p> <p>1 products that have lower risks than existing 2 cigarettes.</p> <p>3 I highlight the word "encourage" because if 4 we're not careful, the burdens imposed by a 5 regulatory scheme or other mechanisms could, in 6 fact, discourage that development. And I think 7 that's a wrong way to go. They should encourage 8 those products to market and then allow the 9 establishment over time in post-market surveillance 10 that the products do, in fact, deliver as the 11 pre-market evaluation suggested that they would.</p> <p>12 The marketing of tobacco products should be 13 consistent with constitutional protections and 14 enhance an adult consumer's ability to make 15 informed choices on risks and comparative risks. 16 And as we've heard already this morning, there are 17 certainly lots of indications where that's perhaps 18 not being done by government-mandated warnings and 19 other public statements by many that do not support 20 the informed choice on risk and relative or 21 comparative risk. And we believe that the 22 prohibition of tobacco products is neither</p>	<p style="text-align: right;">Page 103</p> <p>1 So you have to have a huge study design to be able 2 to pick that up in a prospective manner.</p> <p>3 Our view is that that's probably more 4 appropriately done by a consortium, perhaps via the 5 CTP's PATH study or perhaps a multi-stakeholder 6 effort to set up a prospective epidemiology that 7 can pick up that movement as we go forward in time. 8 That should not be done and cannot be done 9 efficiently, in our view, by individual companies 10 doing their own work, looking for the penetration 11 of a single product here or a single product there.</p> <p>12 We've also heard some today and yesterday 13 about populations at high risk, non-adult 14 consumers, non-traditional consumers in general, 15 but certainly non-adults. That is an area that 16 we're aware that FDA had indicated a need for 17 information there. We have tried to seek clarity 18 from the agency on what that should look like. We 19 have developed tools, in fact, that could be used 20 in non-adult consumers, but we have made it clear 21 with the agency that we will not do that research 22 until we get clear direction from FDA that we must</p>
<p style="text-align: right;">Page 102</p> <p>1 practical nor desirable.</p> <p>2 So when we look at the evidence domains, 3 first of all, these are the IOM recommended 4 evidence domains for modified-risk tobacco 5 products. There are seven. You can read them for 6 yourself. We'll go through those in a moment.</p> <p>7 But what I'd like to point out is that at 8 least under the RAI tobacco operating companies, 9 we're already actively engaged in five of those 10 seven domains: the preclinical, clinical, abuse 11 potential, consumer and non-consumer perceptions, 12 and also, modeling and synthesis.</p> <p>13 There are other research areas that could be 14 more problematic for direct industry sponsorship. 15 One is epidemiology. That is not a classic 16 strength of the tobacco industry. We have explored 17 the notion of prospective epidemiology, but there's 18 broad scope there. That strikes us as something, 19 particularly as you imagine a modified-risk tobacco 20 product that might emerge in the marketplace, you 21 would expect there would be very low penetration 22 early on. It would be difficult to follow that.</p>	<p style="text-align: right;">Page 104</p> <p>1 do that research and we agree on a protocol.</p> <p>2 So you've heard that in various shades over 3 the last two days. That is an area that could be 4 problematic for direct industry sponsorship.</p> <p>5 The second area of the IOM recommendations 6 that I'd like to look at is their recommendations 7 on study governance. So I've briefly highlighted 8 that here in three areas: the independent 9 oversight and conduct, the proper conduct of 10 research, and the public disclosure of research. 11 And you've seen these in one form or another 12 several times over the last few days.</p> <p>13 There's been good discussion certainly under 14 the first bullet about third parties should be 15 preapproved by FDA. Others have disagreed with 16 that notion, and we disagree with that notion. I 17 think if you set up the proper conduct of studies, 18 you should not mandate who can do those studies. 19 You establish the quality and performance criteria, 20 and any vendor who meets those criteria should be 21 able to be used.</p> <p>22 The proper conduct of research, obviously,</p>

<p style="text-align: right;">Page 105</p> <p>1 there are standards and principles of good research 2 guidance, an ethical view that we clearly believe 3 should be adhered to. And then the third 4 recommendation that IOM suggests is that 5 modified-risk tobacco products sponsors should be 6 required to place all data in a public repository. 7 So quickly through our view of those 8 recommendations. In our view, there is no such 9 model of governance in any other regulated 10 industry. The domain space of pre-market-specific 11 product application, in our view, is one solely 12 occupied by the FDA and the product sponsor, and 13 that is very clearly our view. 14 So based on that, the industry has the right 15 and the responsibility to develop that pre-market 16 application for its own products, and that will 17 include various elements of research. But more 18 importantly, FDA has the right and the 19 responsibility to review and approve that research. 20 So what does that mean? In the current day 21 and age, since 2009, FDA has full transparency to 22 the work that we do for products that are in scope</p>	<p style="text-align: right;">Page 107</p> <p>1 Back to public disclosure, I think there are 2 problematic issues around that, particularly in the 3 pre-market stage. We're not aware of any 4 requirement for disclosing such research in any 5 other FDA-regulated industry. It's certainly 6 problematic if it does not protect proprietary 7 information and the ability to innovate, and, 8 again, must work both ways. 9 So what's our approach to governance? The 10 independent oversight and conduct bullet of IOM's 11 recommendation. All work currently undertaken by 12 any of the RAI tobacco operating companies that 13 might support a modified-risk tobacco product 14 application is already done in conjunction with 15 third-party research organizations, whether it's 16 preclinical chemistry, or in vitro toxicology, or 17 in vivo toxicology, or clinical trials, or consumer 18 perception of claims, we already work with 19 third-party research organizations. 20 Those in many cases, and I would even say 21 most cases, are also firms that work on pre-market 22 approval processes with FDA in other regulated</p>
<p style="text-align: right;">Page 106</p> <p>1 for regulation under the Tobacco Control Act. The 2 type and the scope of studies, the protocols, the 3 raw data, algorithms used to generate the results, 4 marketing claims, that is all clearly within their 5 area of responsibility. 6 I've heard the word "transparency" a few 7 times in my life, actually a few times here over 8 the last couple of days. I give you my view of 9 that transparency as we go down to public 10 disclosure and then, particularly, the last bullet 11 that says "any model that precludes industry as 12 stakeholders is unworkable." 13 Transparency is the full transmission of 14 light in both directions. So if you think of a 15 barrier like a piece of glass, that's a clear and 16 colorless piece of glass that transmits light 17 equally in both directions. It's not a 18 half-mirrored glass. And I think in many cases, 19 that's what we have today. So we believe we are 20 rightfully and responsibly stakeholders in this 21 debate, and we will advocate to maintain that seat 22 at the table.</p>	<p style="text-align: right;">Page 108</p> <p>1 industries. So we're using the same partners that 2 FDA is used to working with. 3 In proper conduct of research, all of our 4 work is conducted by qualified researchers and is 5 governed by everything that you would expect it to 6 be governed by: written protocols, contracts that 7 specify data retention policies, statistical 8 analysis plans mentioned earlier and ethical review 9 where appropriate for human work. 10 What does that mean? That means that the 11 laboratories we use are either accredited. Many of 12 them operate according to GLP, and certainly all of 13 our human clinical trials are conducted in 14 accordance with GCP. FDA has full visibility to 15 any and all of that for currently regulated 16 products that it desires. They have much of that 17 data through a variety of processes already, so 18 there is full transparency there that they already 19 have and can exercise and will exercise into the 20 future. 21 So just in summary, some issues with 22 third-party governance, there's no precedent model</p>

<p style="text-align: right;">Page 109</p> <p>1 in any other FDA-regulated industry. There's 2 certainly the potential for the industry and the 3 FDA rights and responsibilities to be relinquished 4 if governance is sort of contracted out to a third 5 party. And in our view, it certainly maintains and 6 furthers the tobacco critics' desire to denormalize 7 the industry rather than treat the tobacco industry 8 as a legitimate stakeholder.</p> <p>9 But there are some opportunities as well. 10 We realize that. Certainly, you could improve the 11 quality of modified-risk tobacco product-related 12 research by opening access to more academicians, 13 perhaps more CROs, journals for publication of 14 research than is currently the norm today.</p> <p>15 You could improve the transparency for all 16 MRTP-related research, no matter which way it's 17 coming from, no matter which side of that glass it 18 starts on, both conducted by industry and also 19 conducted by non-industry. And you could ensure 20 that all stakeholders have an appropriate forum for 21 dialogue and for engagement to share their views 22 and work out the difficulties and the issues in</p>	<p style="text-align: right;">Page 111</p> <p>1 actually suing the FDA, saying that it goes beyond 2 what they should be allowed to do?</p> <p>3 DR. OGDEN: Just like myself, I'm a private 4 citizen. Our company is a corporate citizen. And 5 any agency or any corporate entity has the right to 6 make sure that their rights are protected, to make 7 sure the law is being followed appropriately and 8 not overstepped.</p> <p>9 MR. MYERS: So how is FDA supposed to deal 10 with you in a transformative situation where the 11 organization you're representing says it's illegal, 12 from your point of view, for them to even consider 13 the broad public health measures that are at the 14 heart of this dialogue?</p> <p>15 DR. OGDEN: I'm not sure what you mean by 16 the broad public health --</p> <p>17 MR. MYERS: The public health standard that 18 underlies the very discussion that we're having. 19 I'm just trying to understand how that dialogue 20 takes place when in one breath you're saying we're 21 transformative, we're concerned about these public 22 health measures, and in another breath, the</p>
<p style="text-align: right;">Page 110</p> <p>1 front of them.</p> <p>2 So in conclusion, industry already does most 3 of what IOM recommends. Some of those IOM 4 recommendations appear to be unreasonable and 5 unworkable in some cases, and the independent 6 third-party governance not needed, but 7 collaboration could benefit some areas, again, as 8 long as all stakeholders are appropriately 9 involved.</p> <p>10 Thank you. 11 (Applause.)</p> <p>12 MS. DILLEY: Time for one or two questions.</p> <p>13 MR. MYERS: Matt Myers with the Campaign for 14 Tobacco-Free Kids.</p> <p>15 In talking about the transformation of the 16 industry and its approach, do you think it's 17 appropriate for FDA to consider the broad public 18 health issues that are raised?</p> <p>19 DR. OGDEN: The broad public health?</p> <p>20 MR. MYERS: The public health standard.</p> <p>21 DR. OGDEN: Oh, absolutely. Yes.</p> <p>22 MR. MYERS: Then why is your company</p>	<p style="text-align: right;">Page 112</p> <p>1 institution you represent says to the FDA the very 2 consideration of the public health considerations, 3 this public health standard, violates our legal 4 rights. I'm just trying to figure out how that 5 dialogue --</p> <p>6 DR. OGDEN: Well, I'm not familiar with the 7 exact case of which you speak, even if there is 8 such a thing, so I couldn't address that.</p> <p>9 MR. MYERS: Well, in Kentucky, you sued, and 10 among the many things you challenged was not only a 11 bunch of First Amendment issues, but the very legal 12 standard -- the consideration of the public health 13 standard is one of the core issues raised by your 14 company.</p> <p>15 So I'm just trying to figure out how that 16 dialogue takes place and whether you --</p> <p>17 DR. OGDEN: I'm not a lawyer. You are. I'm 18 a chemist. But it strikes me as reasonable, as 19 everyone has acknowledged, the public health 20 standard is something new. It's new for FDA. It's 21 new for us. It doesn't strike me as unreasonable 22 as a chemist to ask the question is that a fair</p>

<p style="text-align: right;">Page 113</p> <p>1 standard, and perhaps it is. That's fine. But</p> <p>2 it's worth, I think, asking the question to make</p> <p>3 sure that it is what is intended by the Act. It</p> <p>4 does reflect Congress' intent, and it is consistent</p> <p>5 with the laws of the land.</p> <p>6 MS. DILLEY: All right. One more question,</p> <p>7 and then we need to move to the next presenter.</p> <p>8 DR. BACKINGER: Cathy Beckinger, CTP.</p> <p>9 Mike, you said I think on the summary slide,</p> <p>10 improved transparency for all MRTP-related</p> <p>11 research, including that conducted by non-industry</p> <p>12 parties. Just a clarification, could you</p> <p>13 maybe -- I'm not sure exactly what you meant there.</p> <p>14 Transparency for whom? Because you did mention</p> <p>15 that, obviously, it's transparent to FDA. So I</p> <p>16 wasn't sure who you meant transparency for as well</p> <p>17 as plans for transparency on the research that RAI</p> <p>18 is conducting.</p> <p>19 DR. OGDEN: That's a good question. I think</p> <p>20 I can easily clarify that. I think in the</p> <p>21 pre-market world, as I've said, I think that domain</p> <p>22 belongs to the sponsoring company and the FDA. In</p>	<p style="text-align: right;">Page 115</p> <p>1 effects from multiple studies coming from multiple</p> <p>2 stakeholders, FDA should have the ability to see</p> <p>3 all of that data at the same level of detail.</p> <p>4 MS. DILLEY: And you were specific to post-</p> <p>5 surveillance data?</p> <p>6 DR. OGDEN: And it's clear in post-market</p> <p>7 surveillance. There may be some applications in</p> <p>8 other areas, but that one is the most obvious.</p> <p>9 MS. DILLEY: And you'll be returning, Mike,</p> <p>10 for the panel Q&A session.</p> <p>11 DR. OGDEN: Sure.</p> <p>12 MS. DILLEY: So next is Justine Williamson</p> <p>13 who's the head of biosciences at British American</p> <p>14 Tobacco.</p> <p>15 Presentation -- Justine Williamson</p> <p>16 DR. WILLIAMSON: Good morning, everyone.</p> <p>17 I'd like to thank the CTP for giving us the</p> <p>18 opportunity to take part in this very interesting</p> <p>19 workshop. I think none of us are going to be left</p> <p>20 in any doubt that the tobacco industry history as</p> <p>21 laid out in the IOM report has had considerable</p> <p>22 influence on the recommendations that they have put</p>
<p style="text-align: right;">Page 114</p> <p>1 the post-market world, that's different. The</p> <p>2 product would be on the market with an initially</p> <p>3 cleared or approved claim, and I think at that</p> <p>4 point, you would draw a lot of research interest.</p> <p>5 We've seen that with products we've introduced.</p> <p>6 People pick them up at the market. They follow.</p> <p>7 They do Internet-based surveys, et cetera.</p> <p>8 So what I'm imagining there is in a</p> <p>9 post-market surveillance world where the sponsoring</p> <p>10 company has requirements for post-market</p> <p>11 surveillance, you would see post-market</p> <p>12 surveillance emerge from other stakeholders,</p> <p>13 perhaps academicians, perhaps our competition. And</p> <p>14 those types of studies would get published.</p> <p>15 So my point there is if those data are to be</p> <p>16 considered by FDA as to whether to continue the</p> <p>17 support or clearance of a modified-risk claim, then</p> <p>18 all of that data should be in the same full</p> <p>19 transparency mode as the industry data.</p> <p>20 So in other words, they shouldn't rely on</p> <p>21 posters at a meeting or even peer-reviewed</p> <p>22 publications. If we're going to look at the</p>	<p style="text-align: right;">Page 116</p> <p>1 in place. And as a tobacco industry scientist</p> <p>2 today, I must say that history makes uncomfortable</p> <p>3 reading. It has left us with a difficult legacy</p> <p>4 and a more challenging working environment.</p> <p>5 I think sort of two main drivers that really</p> <p>6 stick out are there is a total distrust, obviously,</p> <p>7 of tobacco-sponsored research; and, secondly, that</p> <p>8 there is a belief that the tobacco industry lacks</p> <p>9 the expertise, the infrastructure, the credibility</p> <p>10 to put together a credible and legal MRTP</p> <p>11 application.</p> <p>12 So what I'd like to do today is speak to</p> <p>13 those two drivers from a BAT point of view,</p> <p>14 highlighting some of our experiences over the last</p> <p>15 five to 10 years, and I'll cover these areas.</p> <p>16 Talking about BAT scientists today -- and</p> <p>17 I'll use my own department as an example. So it's</p> <p>18 a biosciences department. There are about 60 of us</p> <p>19 in the department, and we're responsible for the</p> <p>20 majority of British American Tobacco's biological</p> <p>21 testing. So that's from in vitro tox testing,</p> <p>22 through to smoking topography, through to clinical</p>

<p style="text-align: right;">Page 117</p> <p>1 studies.</p> <p>2 Now, two things to note about these guys is</p> <p>3 their average age is 37 and a half, and the average</p> <p>4 length of service at BAT is eight and a half years.</p> <p>5 And these guys, pretty much all, bar one or two,</p> <p>6 including myself, joined British American Tobacco</p> <p>7 post-2000, at a time when the company was</p> <p>8 acknowledging the health risks associated with</p> <p>9 smoking, and had on its corporate website that</p> <p>10 smoking was the cause of serious and fatal</p> <p>11 diseases, lung cancer, COPD and heart disease.</p> <p>12 Also, these guys joined an R&D that had, and still</p> <p>13 has, very active reduced tox programs and harm</p> <p>14 reduction programs.</p> <p>15 So in terms of the expertise that we</p> <p>16 have -- and now we'll talk about my own guys and in</p> <p>17 the wide R&D. I've split this into three areas,</p> <p>18 and I'll start by talking about the historical</p> <p>19 expertise we have.</p> <p>20 So we've had an R&D in Southampton for over</p> <p>21 50 years, so we actually have decades of experience</p> <p>22 in some areas: combustion science, smoking</p>	<p style="text-align: right;">Page 119</p> <p>1 that expertise to start looking at biomarkers,</p> <p>2 in vitro models of disease, clinical studies.</p> <p>3 Now, at the same time, as a company, we were</p> <p>4 looking at how we develop products along the risk</p> <p>5 continuum, and we bought a smokeless tobacco</p> <p>6 company, a Swedish one, and we moved into snus. So</p> <p>7 this was a time for us also then, as we're moving</p> <p>8 into this area, to become familiar with smokeless</p> <p>9 tobacco science.</p> <p>10 So now, more recently, we understand it's</p> <p>11 obviously not just enough to understand what the</p> <p>12 reduced-risk products potentially can do for a</p> <p>13 consumer in terms of individual disease risk, we</p> <p>14 also now need to understand what that's going to do</p> <p>15 to consumer behavior and population effects,</p> <p>16 population health as a whole.</p> <p>17 So all of us -- and we've heard today -- are</p> <p>18 sort of moving into these new areas. We're all</p> <p>19 sort of finding our way a little bit. And so risk</p> <p>20 perception, market surveillance, I should have on</p> <p>21 here abuse liability, are all areas we're starting</p> <p>22 to come to terms with and work out what we should</p>
<p style="text-align: right;">Page 118</p> <p>1 topography, toxicology. And some very good</p> <p>2 fundamental research has come out of that time. I</p> <p>3 think probably many of you in this room are</p> <p>4 familiar with the work of the late Richard Baker</p> <p>5 whose seminal work on combustion science, twice</p> <p>6 published in Nature, really helped at that time in</p> <p>7 understanding the fundamentals of the complexity of</p> <p>8 smoke.</p> <p>9 Then obviously with the publication in 2001</p> <p>10 of the IOM's Clearing the Smoke, this brought on a</p> <p>11 new era in tobacco science because it was then we</p> <p>12 knew it wasn't -- it's not enough just to reduce</p> <p>13 toxicants in products. What that told us to do is</p> <p>14 it told us to show -- we need to show how that</p> <p>15 links to reduced exposure and then how that in turn</p> <p>16 links to actual reduced disease risk.</p> <p>17 So this was a complex and daunting challenge</p> <p>18 probably for all of us and led to a huge expansion</p> <p>19 and diversification of our research programs. We</p> <p>20 didn't have the expertise in house to do that, so</p> <p>21 we had to recruit from the pharma, medical,</p> <p>22 government, academic backgrounds to be able to get</p>	<p style="text-align: right;">Page 120</p> <p>1 be doing around these.</p> <p>2 Most of you know as well that British</p> <p>3 American Tobacco, we have a wholly-owned subsidiary</p> <p>4 company, Nicoventures, a nicotine company. We've</p> <p>5 recently bought an e-cigarette company,</p> <p>6 CN Creative, and we are developing e-cigarettes in</p> <p>7 house as well. So e-cigarette science, again, is</p> <p>8 an area of expertise that we are coming up to speed</p> <p>9 on, really, as fast as we can.</p> <p>10 We've been using the word "transparency" a</p> <p>11 lot, and it's good, so I'm using it on my next four</p> <p>12 slides. So I think that it's viewed by some and it</p> <p>13 was highlighted in the IOM's report that the</p> <p>14 industry is profoundly isolated from the mainstream</p> <p>15 scientific community. And one of the examples that</p> <p>16 is given is that many journals will not accept or</p> <p>17 publish tobacco-funded research.</p> <p>18 Now, of the 24,000 or so journals that are</p> <p>19 out there, approximately a third are science,</p> <p>20 technical/medical journals, and to our</p> <p>21 calculations, we think there are roughly around 9</p> <p>22 or 10 that have explicit bans on publishing</p>

<p style="text-align: right;">Page 121</p> <p>1 tobacco-sponsored research. Thankfully, from our 2 experience, the vast majority of journals judge a 3 manuscript on its scientific merit and not on the 4 funding source.</p> <p>5 So with that said, we've over the past five 6 years published about 100 papers in over 45 7 journals. And the areas we're publishing on are 8 very much associated with some of the questions 9 that the CTP are asking, their 56 priority 10 questions, and very much are hopefully going to 11 help add to the tobacco science, regulatory science 12 field as a whole.</p> <p>13 We have at least 20 of our top scientists, 14 regular referees for over 40 journals. And, 15 ironically, one of the journals that won't accept 16 our publications will accept our free expert labor 17 to review manuscripts.</p> <p>18 (Laughter.)</p> <p>19 DR. WILLIAMSON: Conferences, we go to 20 numerous conferences. We go to tobacco industry, 21 tobacco control, public health, and niche 22 scientific conferences like analytical chemistry,</p>	<p style="text-align: right;">Page 123</p> <p>1 journals very much now so people can get hold of 2 those posters on there. And year and year, we're 3 seeing an increase in interest in the site. Last 4 year, we had 82,000 visitors and 282,000 hits.</p> <p>5 Finally on transparency, we have a visitors 6 welcome policy at our R&D center in Southampton. 7 And we're not just having our own company, BAT 8 staff, come down to understand more about tobacco 9 science and the research we're doing. Of the 34 10 groups that came to us last year, two-thirds of 11 them were external visitors. So that included 12 external scientists, included publishers, 13 regulators, politicians, journalists, analysts, a 14 whole broad range of people coming through.</p> <p>15 The popularity for people to come down and 16 learn about what the tobacco industry is doing in 17 research has meant we've now developed interactive 18 science exhibition and lab tools, all of which are 19 staffed and led by our practicing scientists.</p> <p>20 Over the years, we've hosted a number of 21 external meetings. And we've recently had 22 completed a 300-seat auditorium, so we've been able</p>
<p style="text-align: right;">Page 122</p> <p>1 toxicology, those sort of areas.</p> <p>2 Why do we go to conferences? The same 3 reason as any other researcher goes to conferences, 4 is to inform our research. It's to ensure we're at 5 the cutting edge of research. It's for the 6 continuous professional development of our 7 scientists. And it's also to ensure that our 8 science is out there and is up for scrutiny from 9 the external scientific community.</p> <p>10 On the flip side, we feel we have expertise, 11 knowledge, data that others are interested, 12 especially as this tobacco regulatory science field 13 is growing. And just last week, we were at the SOT 14 and SRNT with seven posters on priority toxicants, 15 clinical studies, in vitro models of exposure, so 16 all things that are of relevance to some of the 17 things we've been talking about today.</p> <p>18 Very quickly, we've had our dedicated BAT 19 science website for about five years, giving an 20 overview of our harm reduction research programs. 21 All of our publications are referenced on there, 22 and where possible, we try to go for open access</p>	<p style="text-align: right;">Page 124</p> <p>1 to host larger conferences. We hosted the British 2 Carbon Group conference last year, and in May, 3 we'll be hosting the In Vitro Testing Industrial 4 Platform meeting.</p> <p>5 So I think what we've found when it comes to 6 research partners is that our sort of decades' long 7 effort to be as open and transparent as we can be 8 has helped when research partners are considering 9 whether they would like to work or collaborate with 10 us. So in terms of -- and what we're finding is 11 that being transparent around our harm reduction 12 approach and our commitment to developing and 13 assessing reduced risk products has meant that high 14 quality CROs are willing to work with us and 15 co-publish with us.</p> <p>16 Academic research organizations, yes, this 17 is more of a sticky one. And the bans in certain 18 universities in the U.K. and the U.S. do mean we 19 have not been able to work with some research 20 groups we would perhaps like to. But we know that 21 the global scientific community grows ever 22 stronger. And though we would like to be funding</p>

<p style="text-align: right;">Page 125</p> <p>1 research in our own background, we can go to 2 expertise literally around the world now. And over 3 the past five, six years, we've had at least 15 4 academic research collaborations going. 5 There's some question about the credibility 6 of research organizations, academic organizations 7 that take funding. And we've co-published with 8 Cornell, with the Max Planck Institute in Germany, 9 and with Cambridge University in the U.K. So I 10 think they would consider themselves to be 11 credible. 12 Commercial partners, yes, we do a little 13 work with commercial partners. My own group right 14 now, I'm working to help characterize a primary 15 human lung cell type to work out the metabolic 16 competency of that. We'll co-publish with those 17 partners. We're also organizing a ring trial of an 18 in vitro health smoke exposure commercially 19 available system with a number of partners, 20 including the supplier. 21 We've been a strong member of CORESTA for 22 many years and do believe that -- this is the</p>	<p style="text-align: right;">Page 127</p> <p>1 able to get up to high regulatory standards. And 2 we have just had -- we're going through a huge 3 overhaul of our quality management and IT systems, 4 recruiting guys from pharma to help us do this in 5 order to meet those standards. 6 Others have touched on disclosure of data. 7 Yes, we agree. We would similarly support the 8 principal of disclosing data, have been discussing 9 that pretty much since we had our website. So 10 again, happy to discuss that. 11 So similarly to the other guys, with the 12 correct governance that the FDA have used for 13 pharma industry, with all this correct governance 14 in place, we don't actually necessarily see the 15 need for independent, third-party research for the 16 majority of research. However, as agreed by the 17 other guys in the industry, consideration for 18 specific areas like vulnerable groups, research on 19 adolescents, then, yes, we should look at that. 20 So to summarize then, we are a new 21 generation of tobacco -- and I should say tobacco 22 and nicotine, now, industry scientists, and we are</p>
<p style="text-align: right;">Page 126</p> <p>1 scientific industry group, and we do believe it's a 2 strong forum for developing good analytical, good 3 technical methods that, again, will be of interest 4 to the tobacco regulatory science field. 5 We've been invited into multi-sector expert 6 groups, and this is because the breadth of our 7 research is growing. So that's with pharma, 8 cosmetic, industrial-type partners. 9 We see the TCORS and the NIH funding 10 opportunities as an excellent way to add to the 11 research base that's going to drive tobacco 12 regulation. And what we would say is that any 13 people interested in sharing any of our expertise 14 or analytical services, or products, we're happy to 15 discuss those types of partnerships. 16 So moving onto governance and similarly to 17 what the first two speakers have said, our research 18 governance includes registration of clinical 19 trials. So it includes oversight of our clinical 20 studies with ethics committees. We only work with 21 CROs to the highest GxP standards, and we have been 22 moving to increase our own internal standards to be</p>	<p style="text-align: right;">Page 128</p> <p>1 determined to leave a more positive legacy than our 2 predecessors. We believe we have significant 3 expertise growing in other areas, and because of 4 our sort of transparent approach, we believe we can 5 engage with enough experts to be able to, in time, 6 produce the credible data that the FDA would like 7 to see. 8 Our views are very much in alignment and 9 agreement with the vast majority of the IOM's 10 views, and, as I said, with correct governance in 11 place. So independent third-party research is 12 probably only required for those sort of certain 13 areas that have already been discussed. 14 So I think that's just about me. And I 15 think probably just to finish, I would agree that 16 we are moving into a new era. And it's my personal 17 opinion that this new era with new regulatory 18 environment, new products, new people mean that all 19 the ingredients are in place now for us to really 20 make a positive impact on tobacco science and 21 public health. 22 Thank you.</p>

<p style="text-align: right;">Page 129</p> <p>1 (Applause.)</p> <p>2 MS. DILLEY: Quick one or two questions.</p> <p>3 David.</p> <p>4 DR. ASHLEY: Thanks. I was very interested</p> <p>5 in the diagram you had on your second or third</p> <p>6 slide about kind of the changes of research and how</p> <p>7 there was traditional research, and you've been</p> <p>8 adding -- you've been moving into new areas.</p> <p>9 In relation to that, are you-all continuing</p> <p>10 to do developmental research on smoke products, or</p> <p>11 have you pretty much moved beyond that and are</p> <p>12 really looking at new products and new directions?</p> <p>13 DR. WILLIAMSON: Yes, we have programs in</p> <p>14 all areas. So we are looking to reduce the</p> <p>15 toxicants within our combustible products, as well</p> <p>16 as looking at developing reduced risk -- well,</p> <p>17 hopefully reduced risk -- smokeless tobacco</p> <p>18 products and nicotine and e-cigarettes, so across</p> <p>19 the board.</p> <p>20 MS. DILLEY: One other question? Anyone?</p> <p>21 (No response.)</p> <p>22 MS. DILLEY: Thanks, Justine. We'll have</p>	<p style="text-align: right;">Page 131</p> <p>1 independent third parties to undertake one or more</p> <p>2 key functions, including the design and conduct of</p> <p>3 research, the oversight of specific studies, and</p> <p>4 the distribution of sponsored funds for research.</p> <p>5 Such independent third parties should be approved</p> <p>6 by the FDA in advance of the research." And that's</p> <p>7 the end of the quote.</p> <p>8 The IOM report also describes several</p> <p>9 governance models, although it acknowledged that</p> <p>10 those models have not been traditionally used in</p> <p>11 product-specific applications.</p> <p>12 The IOM report raised several</p> <p>13 considerations, and we've heard a lot about those</p> <p>14 over the last couple days for industry-sponsored</p> <p>15 tobacco research. To Justine's point,</p> <p>16 transparency; independence of researchers from</p> <p>17 industry influence; use of established research</p> <p>18 methodologies and principles; ethical study</p> <p>19 conduct, including human subject protections; and</p> <p>20 mechanisms to ensure data accuracy and data</p> <p>21 integrity.</p> <p>22 The common underlying theme is ensuring that</p>
<p style="text-align: right;">Page 130</p> <p>1 you come back up when the full panel and respond to</p> <p>2 Q&A.</p> <p>3 So our next speaker is Jeffrey Walker who's</p> <p>4 with Altria Client Services.</p> <p>5 Presentation -- Jeffrey Walker</p> <p>6 DR. WALKER: Good morning. My name is Jeff</p> <p>7 Walker. I'm the vice president and the chief</p> <p>8 medical officer at Altria Client Services, speaking</p> <p>9 today on behalf of Philip Morris U.S.A. and U.S.</p> <p>10 Smokeless Tobacco Company. I want to thank the</p> <p>11 agency for the opportunity to speak today in</p> <p>12 reference to third-party governance of industry</p> <p>13 sponsored research.</p> <p>14 In 2011, the IOM published its report on the</p> <p>15 scientific standards for the evaluation of MRTPs.</p> <p>16 In this report, as we know, the IOM recommended the</p> <p>17 establishment of a third-party tobacco research</p> <p>18 governance entity for studies to evaluate MRTPs.</p> <p>19 The report states that the role of governance is to</p> <p>20 ensure the proper conduct of research.</p> <p>21 Recommendation 10 from the IOM states, and I'll</p> <p>22 quote this, "MRTP sponsors should consider use of</p>	<p style="text-align: right;">Page 132</p> <p>1 the industry-sponsored research results in</p> <p>2 accurate, unbiased, and scientifically relevant</p> <p>3 data that enables FDA to make informed regulatory</p> <p>4 judgments.</p> <p>5 The regulatory framework established by the</p> <p>6 FSPTCA, the Family Smoking Prevention and Tobacco</p> <p>7 Control Act, provides the necessary elements of</p> <p>8 governance to ensure that industry-sponsored</p> <p>9 research meets the expectations and requirements of</p> <p>10 the agency as it implements its regulatory</p> <p>11 authority.</p> <p>12 As such, third-party governance is</p> <p>13 duplicative and unnecessary in light of the</p> <p>14 agency's regulatory authority. This does not mean</p> <p>15 we oppose the use of third parties. Rather, it's</p> <p>16 the proposed governance by third parties that we</p> <p>17 consider problematic. As I will discuss, third</p> <p>18 parties are currently serving important roles and</p> <p>19 will continue to do so.</p> <p>20 I would like to address first how FDA can</p> <p>21 apply its authority, its knowledge, and its</p> <p>22 processes to provide the governance of tobacco</p>

<p style="text-align: right;">Page 133</p> <p>1 industry-sponsored research. Under the FSPTCA, 2 Congress granted FDA broad authority and broad 3 enforcement authority over manufacturing and 4 marketing of new and modified-risk tobacco 5 products, including pre-market authorization 6 authority. FDA can also provide direction, 7 oversight, and guidance to sponsors for the conduct 8 of tobacco research.</p> <p>9 With regard to transparency, the FSPTCA 10 created a regulatory framework that requires 11 industry openness and interaction with the FDA. 12 Since June of 2009, the agency has access to 13 manufacturing facilities, product formulas, and 14 information relating to the production and other 15 aspects of regulated tobacco products. The agency 16 has authority for and has conducted unannounced 17 site visits to manufacturing facilities. The 18 agency has also conducted site visits of tobacco 19 product research and manufacturing facilities to 20 learn more about the industry.</p> <p>21 In addition, the FDA has authority under 22 Section 904 of the FSPTCA to access an extensive</p>	<p style="text-align: right;">Page 135</p> <p>1 With regard to scientific standards for the 2 breadth and conduct of industry-sponsored research, 3 the IOM report stated that the industry lacks the 4 ability to produce comprehensive and credible data 5 about tobacco products. This perspective fails to 6 consider the agency's role and their ability to 7 establish and apply scientific standards to tobacco 8 industry-sponsored research in support of product 9 applications.</p> <p>10 The FDA has tremendous expertise in 11 regulating a wide variety of companies across the 12 food, drug, dietary supplement, biologic and 13 medical device fields. Many of these companies 14 routinely conduct sponsored research in support of 15 product applications, and the vast majority of 16 these companies conduct high quality, industry- 17 sponsored research that complies with acknowledged 18 standards of preclinical and clinical practice and 19 ethical study conduct through the use of GLP and 20 ICH GCP guidelines. FDA can and I suspect will 21 establish similar standards for the conduct of 22 tobacco industry-sponsored research.</p>
<p style="text-align: right;">Page 134</p> <p>1 and unfiltered array of industry documents 2 pertaining to the health, toxicological, 3 behavioral, or physiologic effects of current or 4 future tobacco products.</p> <p>5 From my 19 years of working in industry, 17 6 years of which I spent working in medical devices, 7 pharmaceutical development and combination 8 products, I've observed industry-sponsored research 9 under FDA regulation is a transparent process. It 10 typically includes sponsor meetings with the agency 11 prior to, during, and following the conduct of a 12 wide range of scientific studies, both preclinical 13 and clinical. The FDA also obtains from sponsors 14 original data, reports and internal findings 15 related to the research and development of new 16 regulated products in pre-market applications.</p> <p>17 In short, FDA implements regulatory 18 processes that assures sponsor provides the agency 19 with data in its unaltered and original form. 20 Under the Act, FDA has an even greater degree of 21 transparency with tobacco-sponsored research than 22 it does with pharmaceutical or medical device.</p>	<p style="text-align: right;">Page 136</p> <p>1 With regard to independent study conduct, 2 other regulated industries use third-party 3 independent, internationally-recognized CROs, 4 contract research organizations, to obtain high 5 quality data that is used by the sponsor in support 6 and by the FDA in the evaluation of pre-market 7 product applications.</p> <p>8 In most stages of research, the CRO is 9 responsible for the selection of high qualified 10 investigators, implementation of study protocols, 11 data monitoring, and quality audits. The CRO can 12 also establish independent data safety monitoring 13 boards, data monitoring committees, and other 14 functions that are independent of sponsor 15 interference.</p> <p>16 In our view, the FDA can apply the knowledge 17 gained from overseeing other industry research and 18 its authority under FSPTCA to enable similar 19 approaches for industry-sponsored tobacco product 20 research.</p> <p>21 With respect to industry engagement, FDA 22 draft guidances on new and modified-risk product</p>

<p style="text-align: right;">Page 137</p> <p>1 applications encourage the sponsors to solicit 2 feedback from FDA on planned studies in support of 3 product applications, including feedback on study 4 design, statistical analysis, data collection, 5 human subject protections.</p> <p>6 The agency has also issued guidance on how 7 industry and investigators can request and conduct 8 such meetings with the agency. These meetings are 9 critical opportunities in the regulatory process, 10 both for the agency to provide research guidance 11 and for sponsors who seek to gain agency feedback 12 on planned studies to support product applications. 13 Effective engagements with FDA on study design and 14 study conduct will enable sponsors to provide FDA 15 the requisite and scientifically relevant data that 16 it needs to evaluate product applications.</p> <p>17 I'd like to turn to the potential role of 18 third parties in industry-sponsored research. 19 First, such interaction is contemplated by the 20 regulatory framework. FDA can and does solicit 21 third-party expertise and input as it implements 22 its regulatory authority. For example, the FSPTCA</p>	<p style="text-align: right;">Page 139</p> <p>1 products in certain populations such as nonusers, 2 former tobacco users, or youth, or in the area of 3 abuse liability.</p> <p>4 Overall, while we don't endorse a single 5 model or approach, we believe that there are 6 several principles that should govern the use of 7 third parties by FDA and by sponsors. First, FDA 8 retains its industry governance and oversight 9 authority. FDA should not abdicate or share this 10 authority.</p> <p>11 Sponsors should retain the responsibility 12 recognized by the FSPTCA to generate and submit to 13 FDA the science and the evidence required for 14 pre-market applications. And sponsors should 15 retain intellectual property rights and protections 16 associated with study results or data analysis as 17 accomplished in other FDA-regulated industries.</p> <p>18 So in closing, third-party governance of 19 tobacco industry-sponsored research is duplicative 20 and could add unnecessary complexity to FDA's 21 regulation of tobacco products. The agency has the 22 expertise and the authority to advance tobacco</p>
<p style="text-align: right;">Page 138</p> <p>1 established a TPSAC, Tobacco Products Scientific 2 Advisory Committee, to provide FDA with advice, 3 information, and recommendations regarding 4 modified-risk applications and other regulatory 5 matters.</p> <p>6 The agency has solicited third-party 7 expertise from the IOM on the topic of standards 8 for modified-risk products. Further, the agency 9 has the authority and the financial resources to 10 solicit input from highly credible and independent 11 sources of scientific expertise that it believes 12 beneficial in the conduct of its duties, including 13 those related to industry-sponsored research.</p> <p>14 Moving forward, both FDA and sponsors could 15 use third parties to develop methods, conduct 16 studies, or analyze data for new or potential 17 modified-risk tobacco products. These third 18 parties may include qualified contract research 19 organizations, independent scientific experts, or 20 academic institutions.</p> <p>21 Third parties may be particularly beneficial 22 in research related to the impact of tobacco</p>	<p style="text-align: right;">Page 140</p> <p>1 product regulation in a science- and evidence-based 2 manner without abdicating its governance authority 3 to a third party.</p> <p>4 However, third parties can serve several 5 important functions. FDA should seek input and 6 expertise from a variety of third parties that can 7 contribute to implementation of its 8 congressionally-mandated authority. Further, the 9 FDA and sponsors could use third parties in a 10 principled way to develop methods, conduct studies, 11 or analyze data related to new or potential 12 modified-risk tobacco products.</p> <p>13 How the agency implements its authority over 14 tobacco products, including its oversight of 15 industry research, is still unfolding. We expect 16 to engage and work constructively with the agency 17 to generate the requisite scientific evidence to 18 support new or modified-risk tobacco products.</p> <p>19 Thank you. 20 (Applause.) 21 MS. DILLEY: A couple of questions? 22 (No response.)</p>

<p style="text-align: right;">Page 141</p> <p>1 DR. WALKER: Thank you.</p> <p>2 MS. DILLEY: Very straightforward. Thank</p> <p>3 you.</p> <p>4 Michael Hufford is our last speaker. He's</p> <p>5 the chief medical officer, e-Nicotine Technology.</p> <p>6 Presentation – Michael Hufford</p> <p>7 DR. HUFFORD: Thanks so much for your time</p> <p>8 and attention today. By way of disclosures, I'm</p> <p>9 co-founder and chief medical officer of e-Nicotine</p> <p>10 Technology, a small healthcare company devoted to</p> <p>11 harm reduction and helping smokers transition off</p> <p>12 of combustible tobacco products to safer, clean</p> <p>13 nicotine products. I also want to note that</p> <p>14 neither myself nor any of my colleagues at</p> <p>15 e-Nicotine Technology have ever been employed by</p> <p>16 nor taken money from the tobacco industry.</p> <p>17 I'm going to be touching on a number of</p> <p>18 points today, both the IOM report. I also am going</p> <p>19 to touch on both the promise and some of the perils</p> <p>20 of using the pharmaceutical drug development as a</p> <p>21 role model for the development of modified-risk</p> <p>22 tobacco products, and end by sharing some thoughts</p>	<p style="text-align: right;">Page 143</p> <p>1 of my perspective on this is also shaped as a drug</p> <p>2 developer.</p> <p>3 Lastly, I've also helped to grow a number of</p> <p>4 specialty contract research organizations focused</p> <p>5 both on electronic patient-reported outcomes and</p> <p>6 neuropsychological assessment in clinical trials.</p> <p>7 So I also wanted to speak from that perspective</p> <p>8 from the trenches much as Donald Graff and Eric</p> <p>9 Donny have done before me.</p> <p>10 So in terms of the IOM report, e-Nicotine</p> <p>11 Technology supports each of the 12 recommendations</p> <p>12 contained in the guidance document. And, indeed, I</p> <p>13 thought it was interesting that that document also</p> <p>14 foreshadowed companies like e-Nicotine Technology;</p> <p>15 we are by no means the only one.</p> <p>16 Getting into this space, we absolutely</p> <p>17 should face the same high rigorous standards for</p> <p>18 scientific conduct and transparency in all of our</p> <p>19 research; although I think it's also the case that</p> <p>20 coming at this, whether you're a pharmaceutical</p> <p>21 company, a biotech company, or a company explicitly</p> <p>22 focused on the development of novel products in</p>
<p style="text-align: right;">Page 142</p> <p>1 on the critical role, I think, that innovation can</p> <p>2 play at an intersection of science and regulation</p> <p>3 to help potentially dramatically transform the</p> <p>4 tobacco control landscape.</p> <p>5 My perspectives on these issues are shaped</p> <p>6 by my experience. I started off as a nicotine</p> <p>7 researcher doing research in cue reactivity and</p> <p>8 using ecological momentary assessment to try to</p> <p>9 better understand the relapse process amongst</p> <p>10 smokers trying to quit. I became disheartened with</p> <p>11 my own research insofar as if you track the number</p> <p>12 of peer-reviewed publications over time but plotted</p> <p>13 against the average abstinence rate, thanks to</p> <p>14 smoking cessation interventions, the two curves</p> <p>15 show remarkably little relationship to one another.</p> <p>16 So I got involved in drug development, and,</p> <p>17 again, some of my perspective is shaped by that</p> <p>18 experience as well. I was fortunate to work in</p> <p>19 both fields of orphan drugs as well as large</p> <p>20 pharmaceutical markets around obesity, also helped</p> <p>21 to get a drug approved, Naprosyn, for the</p> <p>22 management of fibromyalgia through CDER. So some</p>	<p style="text-align: right;">Page 144</p> <p>1 this space, we may not have to overcome the same</p> <p>2 hurdles in maintaining or restoring credibility to</p> <p>3 their research as is noted in the report.</p> <p>4 I also wanted to note the electronic</p> <p>5 nicotine delivery devices I believe should receive</p> <p>6 an appropriately abbreviated and expedited review</p> <p>7 if they're shown to deliver far fewer harmful or</p> <p>8 potentially harmful constituents as compared to</p> <p>9 conventional cigarettes.</p> <p>10 Indeed, the Light Touch regulation, that in</p> <p>11 Britain the medicines and healthcare products</p> <p>12 regulatory agency or MHRA is currently considering,</p> <p>13 I think may be very appropriate to this industry</p> <p>14 and, in fact, in the best interests of public</p> <p>15 health. That Light Touch regulation, in my mind,</p> <p>16 should address a number of critical issues that</p> <p>17 aren't being governed today; so PK data, for</p> <p>18 instance, to know that you're getting a consistent</p> <p>19 dose of nicotine, which is shown to be deficient in</p> <p>20 many current products.</p> <p>21 Evidence of quality manufacturing and batch-</p> <p>22 to-batch reliability. This is known in the</p>

<p style="text-align: right;">Page 145</p> <p>1 pharmaceutical industry as CM&C issues, chemistry, 2 manufacturing and controls. There is no excuse for 3 contaminations like diethylene glycol in a 4 consumer's use of a product that should contain 5 only nicotine and propylene glycol. And, in fact, 6 wearing my drug development hat, that's a fairly 7 easy problem to solve. That's a very tractable 8 problem. 9 So PK data, evidence of quality 10 manufacturing, screening of marketing materials to 11 be used in marketing these products, and 12 post-marketing surveillance, I think would 13 represent a very reasonable regulatory middle 14 ground, enabling innovation to come forward with 15 less harmful products and not stifling the sorts of 16 innovation, which I'm going to talk about in a bit, 17 that I think historically has led to radical 18 transformations in other industries. And I think 19 we're on the precipice of doing just that in this 20 industry as well. 21 I want to talk just a little bit about the 22 pharmaceutical drug development and using contract</p>	<p style="text-align: right;">Page 147</p> <p>1 case that you can find both in the peer reviewed 2 literature and certainly in the blogosphere folks 3 criticizing that act, believing that it creates too 4 cozy a relationship between the pharmaceutical 5 industry and the FDA, or that too many of the funds 6 are used for things other than safety, for 7 instance. 8 I raise all that only to note that at the 9 end, as Voltaire said, "The best should not be the 10 enemy of the good." Almost any action the CTP 11 takes is bound to develop some controversy. Public 12 opinion will land in a variety of -- along a 13 spectrum for almost any actions that you take. 14 Now, three years in to the passage of the Family 15 Smoking Prevention and Tobacco Control Act, I do 16 hope that we can move forward swiftly. 17 I did want to just note one caveat about the 18 perils of the CRO model, though. Many of you may 19 be familiar with Moore's Law. This was a 20 prediction back in the mid-60s, believe it or not, 21 that over the history of computing, that the number 22 of transistors on an integrated circuit would</p>
<p style="text-align: right;">Page 146</p> <p>1 research organizations for some of this research. 2 Again, Donald Graff just did a wonderful job 3 articulating a number of the strengths of the 4 model. I won't belabor that. This is just a plot 5 of the global location of CROs by continent and 6 country. There's tremendous bandwidth here to get 7 this research done. Indeed, this is a \$24 billion 8 industry in 2010, so there's tremendous bandwidth 9 and expertise if we can find an agreeable way to 10 use that expertise to help MRTPs move forward. 11 I in no way envy the CTP's path in front of 12 them insofar as almost any action they take may 13 well be litigated by big tobacco as well as be the 14 subject of considerable public controversy. That's 15 also the case with some very prominent acts that 16 govern CDER and the development of drugs and 17 medical devices. 18 So the Prescription Drug User Fee Act, known 19 as PDUFA, was implemented in 1992 to help speed the 20 review of applications for new drugs to the agency. 21 It has succeeded in doing that. I think the facts 22 largely bear that out. But it's also certainly the</p>	<p style="text-align: right;">Page 148</p> <p>1 double approximately every 24 months. In fact, 2 that has exactly been the case. This is a field 3 that has just innovated time and time again and 4 shown just dramatic and radical innovation. It is 5 testimony to what Alan Kay said, that "the best way 6 to predict the future is indeed to create it." 7 Sadly, when it comes to drug development, 8 the model is almost on its head. This is from a 9 Nature publication by Scannell, et al. They take 10 about Eroom's Law. Eroom's Law is the number of 11 new drugs approved by the FDA per billion of U.S. 12 dollars, inflation adjusted, spent on R&D has 13 halved roughly every nine years. So, 14 unfortunately, when it comes to drug development, 15 the curve goes in the opposite direction. We spend 16 more and more money and take more and more time to 17 get each drug approved. 18 Now, there's a lot of reasons for that I 19 think are shared across the regulatory environment, 20 the scientific environment, as well as the CRO 21 environment. So as we think about relying on CROs 22 for some of that work, we need to be aware this is</p>

<p style="text-align: right;">Page 149</p> <p>1 a crowded space. This also tends to be fairly low 2 margin work in CROs. And so you also have to think 3 about the economic incentives to get companies to 4 choose to do MRTP research versus other 5 pharmaceutical types of research. It's also the 6 case that the costs associated with developing 7 drugs is increasing astronomically.</p> <p>8 I wanted to start to transition, though, to 9 the role of innovation then and how it intersects 10 with the regulatory landscape, and, in particular, 11 this issue of third-party governance and how we can 12 best help modified-risk tobacco products that can 13 potentially meaningfully impact public health move 14 forward as quickly as possible.</p> <p>15 This is from an article by Bernard Munos, 16 Lessons from 60 Years of Pharmaceutical Innovation, 17 showing that, in fact, large companies are 18 increasing responsible for fewer and fewer 19 products. Small companies are responsible for 20 those. I'm going to draw a parallel to big tobacco 21 in just a moment. And another publication also 22 looked at the importance of new companies in drug</p>	<p style="text-align: right;">Page 151</p> <p>1 Prescription. It's very relevant reading because 2 it talks about how large entrenched industries that 3 at one point in history seemed just so impenetrable 4 and formidable can be destroyed by radical 5 innovation that eats away at them from the margins. 6 And, indeed, Clayton Christensen talks about the 7 role of innovation first in industries drives 8 centralization of knowledge and skills. Innovation 9 plays oftentimes a key role in building big 10 business. But then just as predictably, given the 11 right regulatory environment, the right science, 12 and I'm going to argue the right innovation, 13 innovation then plays a reciprocal role in 14 decentralization.</p> <p>15 So we're going to talk a little bit about 16 what that innovation is likely to look like and how 17 regulation can help be sure not to impede that 18 innovation.</p> <p>19 So we're going to talk about there's also an 20 important difference here between radical 21 innovations and incremental innovations. 22 Incremental innovations tend to come out of large</p>
<p style="text-align: right;">Page 150</p> <p>1 discovery and looked at a decade of new products 2 and found, in fact, a majority were coming from 3 biotech companies or university discovered and then 4 transferred to biotech companies. They tend not to 5 come from large industry.</p> <p>6 With that, I'd like to transition and talk a 7 little bit about the role of innovation and its 8 intersection with science and regulation in this 9 field.</p> <p>10 Almost this entire book is quotable, The 11 Structure of Scientific Revolutions from Thomas 12 Kuhn, but I thought this quote was in particular 13 very apropos to the current environment. It says, 14 "As in manufacture, so in science, retooling is an 15 extravagance to be reserved for the occasion that 16 demands it." And I would offer to you that this is 17 absolutely an occasion that demands it.</p> <p>18 In fact, in terms of the retooling, one of 19 the things if you haven't read, I would urge you to 20 take a look at some of the work that Clayton 21 Christensen has published on the Innovator's 22 Dilemma, as well as on healthcare, the Innovator's</p>	<p style="text-align: right;">Page 152</p> <p>1 companies. That's true whether it's the 2 pharmaceutical industry, whether it's the tobacco 3 industry. Radical innovations very often are 4 driven by smaller companies pursuing radical ideas. 5 So who's it new to? Well, radical innovation is 6 new to the world. Incremental innovations are new 7 to the company. The risk profile of radical 8 innovations tend to be high relative to incremental 9 innovations, and there are some unique challenges 10 both in terms of requiring new competencies for 11 radical innovations, destroying existing 12 organizational competencies oftentimes, and 13 oftentimes having to get involved in social and 14 systematic change to bring those innovations about. 15 By contrast, incremental innovations tend to 16 utilize existing skills present in large companies 17 and perpetuate existing social practices.</p> <p>18 Relationship to the status quo. Radical 19 innovations tend to challenge the status quo. 20 Incremental innovations tend not to. But at the 21 end of the day, I think what we need from a public 22 health perspective to help people transition off of</p>

<p style="text-align: right;">Page 153</p> <p>1 these incredibly harmful and, in fact, deadly 2 combustible tobacco products is really a step 3 change in performance versus a gradual performance 4 improvement.</p> <p>5 So I'd like to walk you through what I see 6 as a certain formula here. As Brandt articulated 7 just wonderfully in the Cigarette Century, the 8 cigarette industry, the modern tobacco industry, 9 had a number of dramatic innovations. And I should 10 note that innovation is fundamentally amoral, not 11 that it's immoral but it's amoral. It's really 12 outside the scope of right or wrong. Innovation 13 can accomplish great things, but whether those are 14 good or bad really depends on what direction you 15 point the innovation towards.</p> <p>16 In this case, in the late 1800s, say, you 17 had it pointed toward profit alone. And so the 18 flue-curing of the leaf to change the pH so that 19 the smoke could be taken into the deep lung, which 20 radically accelerated the absorption of nicotine 21 and its activation of the nicotinic alpha-4 beta-2 22 receptors in the brain and dopamine release, that</p>	<p style="text-align: right;">Page 155</p> <p>1 front of us today. This is an image that I took 2 from the World Lung Foundation's Tobacco Atlas. 3 Each pack of cigarettes on this particular slide 4 represents 30 billion cigarettes. I will not 5 attempt to address the epidemiologic disaster that 6 this represents.</p> <p>7 Sir Richard Peto, for those of us who were 8 at the Society for Research on Nicotine and Tobacco 9 last week, did a fantastic job reviewing the 10 epidemiology and the estimated public health impact 11 of this industry in the 21st century, claiming 12 potentially 1 billion lives if something is not 13 done.</p> <p>14 I don't want to belabor that point. What I 15 want to focus on is this other plot from the 16 Tobacco Atlas because I think it plays a key role 17 in how innovation can be leveraged to bring about a 18 dramatic change to this industry. In case you 19 can't read it, this notes that "Tobacco company 20 profits in 2010, the combined profits of the six 21 leading tobacco companies was \$35 billion." That's 22 profits. That was equal to the combined profits of</p>
<p style="text-align: right;">Page 154</p> <p>1 was a radical innovation at the time. The Bonsack 2 machine acquired by the Duke family back in 1881, a 3 radical innovation.</p> <p>4 There have been countless thousands of 5 incremental innovations, including the use of 6 ammonia, for instance, to enhance the addictive 7 profile of some cigarettes.</p> <p>8 So this is what you have. You have a field 9 that had a lot of innovation. And when you combine 10 that with a lack of scientific insight -- that's 11 not a completely accurate descriptor. I think, in 12 fact, as has been well chronicled -- and this 13 particular page is kind of hard to read, but this 14 is from the famous Doubt is Our Product memo. 15 There was a combination of a lack of understanding 16 of causation and lung cancer, in particular, as 17 well as an active obfuscation of some of that data 18 coming out of industry.</p> <p>19 But if you combine that innovation, then, 20 with a lack of scientific insight, combined with a 21 lack of regulatory oversight, well, we 22 fundamentally have the problem that we have in</p>	<p style="text-align: right;">Page 156</p> <p>1 Coca Cola, Microsoft, and McDonalds in 2010.</p> <p>2 Why do I focus on these revenues? This 3 isn't to shame anyone about having a big business. 4 This is because, as Mary Lasker, the noted cancer 5 advocate and philanthropist noted, that "money is 6 frozen energy and that it unfreezes itself when you 7 pay people to work." And the point I want to drive 8 home to you is that is a tremendous amount of 9 frozen energy. That is a market that under the 10 right regulatory framework, I think venture 11 capitalists could potentially flock to.</p> <p>12 Venture capitalists in this 13 country -- venture-based companies provide 14 11 percent of the private sector jobs in this 15 country. The venture-backed companies are 16 responsible for about 21 percent of the U.S. GDP, 17 invest about \$30 billion in these companies.</p> <p>18 I don't know how many of you saw this 19 recently in the news. James Cameron and some 20 Google executives made a venture-backed investment 21 in asteroid mining. Do whatever you want with your 22 money, I suppose.</p>

<p style="text-align: right;">Page 157</p> <p>1 What strikes me about the tobacco industry 2 is in the U.S. alone, it's an \$80 billion industry, 3 responsible for 440,000 deaths per year. This is a 4 potential venture investment that has the rare 5 opportunity to both do good but also do very well. 6 I think it's possible both to save lives and to 7 potentially generate a huge return on investment in 8 innovation in this sector. 9 So now I want to rewrite that formula for 10 you about innovation now pointed in a different 11 direction. These are a variety of different 12 products in a variety of different stages of 13 development. I'd like to note a great quote I came 14 across from Michelangelo. He said, "The greatest 15 danger for most of us is not that our aim is too 16 high and we miss it, but rather that our aim is too 17 low and we reach it." So certainly, a number of 18 innovators in this space, including e-Nicotine 19 Technology, intend not to fail by the latter part 20 of that clause, but if anything perhaps, by the 21 former. 22 So for ourselves, our focus on innovation,</p>	<p style="text-align: right;">Page 159</p> <p>1 that, in fact, nicotine is not a direct 2 carcinogen -- and this is a slide from a 2010 3 meeting on NRTs that the FDA hosted. The figure to 4 the right, by the way, is hard to see here. It was 5 actually created by an ad agency in Saudi Arabia. 6 It lists in microscopic print all 4,000 chemicals 7 listed in a cigarette. It's a great image if you 8 can find it online. It shows up quite better 9 there. 10 So if you combine that innovation with the 11 scientific insight that we now have about nicotine, 12 combined with the newly empowered regulatory 13 oversight, what we have, I think, is still just a 14 tremendous amount of work cut out for us. We still 15 have an enormously large industry. It really is in 16 every sense of the word a Goliath. I suppose like 17 any entrepreneur, I believe, though, that I both 18 have a sling as well as a particularly hard rock. 19 Lastly, I want to note, in terms of its 20 interaction with CTP in particular, I'm not sure 21 how many applications CTP anticipated getting. I 22 was at a session again at SRNT last week talking</p>
<p style="text-align: right;">Page 158</p> <p>1 our products shown here on the left, combines 2 deep-lung deposition of pure nicotine and propylene 3 glycol in a 1 to 3 micron particle to the deep lung 4 to mimic the rapid pulsatile pharmacokinetics of a 5 smoked cigarette. But onboard e-health tools, I 6 think for the first time, enable the user to choose 7 what relationship they want to have to nicotine, 8 whether that's complete or partial, coming off or 9 transitioning off of combustible tobacco products, 10 or weaning off of nicotine entirely. Also, 11 electronic controls enable you to have parental 12 lockouts, enable you to do things like prevent 13 overdose. 14 My point being that research can inform 15 policy. Policy can also inform research. But at 16 the end of the day, tobacco control is about taking 17 action. And action fundamentally can be taken 18 either by big tobacco with incrementally innovative 19 products or other products that they've developed, 20 or it can be taken up by the entrepreneur. 21 So if you combine this innovation, then, 22 with the scientific insight that we have today,</p>	<p style="text-align: right;">Page 160</p> <p>1 about more than 3,000 applications have been 2 submitted. I thought I saw that perhaps 10 of 3 those were MRTPs. So what may have started like 4 that, kind of started looking like this, and from 5 there. 6 This is not a WikiLeaks photo, though I am 7 suspicious that there's a room somewhere in this 8 building that may well look a lot like this. This 9 is sort of the potential to induce drowning via 10 paper. I studied this figure carefully, and I 11 think in the -- I think I saw my meeting request, 12 which is on the bottom. 13 (Laughter.) 14 DR. HUFFORD: So one point I wanted to make, 15 in terms of moving forward with this sort of volume 16 of applications, though, in all seriousness, is a 17 focus on best ideas versus most ideas, because I 18 think fundamentally what we need here is radical 19 innovation versus incremental innovation. 20 So if you imagine a variety of products that 21 have submitted, in fact, clearly hundreds of 22 applications, and if you think about a typical</p>

<p style="text-align: right;">Page 161</p> <p>1 combustible product with numerous different blends 2 of tobacco being used, there's some n factorial 3 number of ways that those products can be combined. 4 So the potential here to sort of drown in 5 applications is likely quite real. 6 You could certainly review them in the order 7 received. I would argue from a public health 8 standpoint, it may be best to review each company's 9 best ideas first. Have either them potentially 10 nominate what they think their best idea is, or 11 perhaps you take that on yourself, which has the 12 potential for the most public health impact. 13 And if you did that, appreciating that each 14 company would have to be partially or wholly-owned 15 subsidiaries -- you don't game the system -- can 16 submit as many of these applications as they have, 17 but the best ideas are nominated and reviewed 18 first, and that that system would have as a 19 virtue -- perhaps not grinding to a halt by virtue 20 of hundreds of incremental applications and also 21 focus on radical innovation, which I'd argue both 22 historically and across multiple industries comes</p>	<p style="text-align: right;">Page 163</p> <p>1 problem on the planet, and I hope that you share 2 our vision of a smokeless world. 3 (Applause.) 4 MS. DILLEY: Thank you, Michael. 5 A couple of questions for Michael before we 6 have the other panel members come up and start our 7 full Q&A session. So question over here. 8 MR. MOYNIHAN: Yes, just a very simple 9 clarifying question. You alluded to a meeting 10 request, so would you mind saying when you 11 submitted it? 12 MS. DILLEY: Could you introduce yourself, 13 by the way, just so we can -- 14 MR. MOYNIHAN: Michael Moynihan, Goodrich 15 Tobacco. 16 MS. DILLEY: Thank you. 17 DR. HUFFORD: I actually submitted it on my 18 birthday, December 5th, so it was a gift to myself. 19 MS. DILLEY: Any other question for Michael? 20 Matt? 21 MR. MYERS: Matt Myers, Campaign for 22 Tobacco-Free Kids. Thanks, that was fascinating.</p>
<p style="text-align: right;">Page 162</p> <p>1 from smaller companies, it would help to ensure 2 that those things have equal access for FDA input 3 and review. 4 So by way of summary, I'd like to reiterate 5 our support for the IOM report on scientific 6 standards for the studies on modified-risk tobacco 7 products. I think there's a lot of potential 8 benefit, some drawbacks, to using the 9 pharmaceutical drug development model to get some 10 of that research done. And as I hope has been 11 clear, I see a key role for innovation in 12 potentially radically transforming this industry. 13 I wanted to end as the IOM report began, 14 with this note, that "Knowing is not enough. We 15 must apply." And that "Willing is not enough. We 16 must do." 17 Despite this being a very different 18 presentation and a very different audience than a 19 typical venture presentation that I might give on 20 behalf of my company, I'd like to end with the 21 exact same observation, which is I firmly believe 22 we're working on the most important drug delivery</p>	<p style="text-align: right;">Page 164</p> <p>1 So you talked a lot about the product 2 innovation. I'm curious, because the second 3 component of what you said in terms -- spoke in 4 terms of your goals was -- if I'm interpreting it 5 right and if I'm wrong, tell me -- moving people 6 from products that kill people to products that you 7 believe don't kill people. 8 DR. HUFFORD: That's correct. 9 MR. MYERS: Which is at the core of the 10 public health standard. So how would you envision 11 doing that as well under your model? 12 MS. DILLEY: You mean doing that -- 13 MR. MYERS: It's the moving piece because 14 MRTP -- the Section 911 looks at the product, but 15 it also looks at what's the population effect of 16 the product. And, therefore, you have to have a 17 plan for the population effect to understand that. 18 DR. HUFFORD: That's a great question. And 19 I was sharing with a colleague just last night the 20 Sumner paper. I may get the journal wrong now. I 21 think it was 2010. It might be Tobacco Control, 22 but it might not be. But Sumner had done some</p>

<p style="text-align: right;">Page 165</p> <p>1 estimates of what a clean nicotine inhaler, what 2 its uptake would do to helping meet the President's 3 Healthy Standards 2010, and found that in many 4 scenarios, that alone would meet those goals. 5 MR. MYERS: But it only meets those goals if 6 people actually switch to your product as opposed 7 to use your product at some times, smoke cigarettes 8 at other times, et cetera. So how do you -- 9 DR. HUFFORD: First of all, even in that 10 scenario, I would argue that there is some public 11 health good taking place, not as much as you would 12 like. But secondarily, as I mentioned, in the 13 Light Touch regulation, post-marketing surveillance 14 of how the product is used, I think should be a 15 burden placed on manufacturers. I think these 16 things would be of tremendous interest to the 17 academic community as well. 18 So I think that's a great role for post- 19 marketing surveillance to fully characterize 20 precisely how the product is used. And I'd also 21 argue that at the end of the day, that's really the 22 only way to do it, is to get in the marketplace and</p>	<p style="text-align: right;">Page 167</p> <p>1 Swedish Match would not be involved in any research 2 among adolescents. What type of governance 3 structure do you think would be appropriate for 4 this type of research that is required by the FDA 5 for MRTTP applications?" 6 DR. RUTQVIST: Well, ideally, I would like 7 that type of research to be conducted by 8 independent university-based research groups. And 9 in such case, the whole issue of governance 10 wouldn't come up. And I think also that that would 11 ensure a very high level of credibility. 12 If such research is not done by that type of 13 group, I think in many of the models that, we've 14 discussed, could be possible, including the models 15 mentioned in the IOM report. And certainly, 16 perhaps some of the models that are discussed in 17 Jim Solyst's research article in the FDLI journal. 18 So there are many options, but, ideally, a 19 totally independent research group. 20 MS. DILLEY: Anyone else want to speak to 21 that particular issue, governance structure for 22 particularly vulnerable or adolescent populations?</p>
<p style="text-align: right;">Page 166</p> <p>1 let those market forces play out and see how the 2 product's actually used. 3 MR. MYERS: So one last question, because 4 you didn't actually say this. Your product 5 currently isn't regulated by FDA. Do you support 6 them being regulated by Light Touch? 7 DR. HUFFORD: I support them being regulated 8 by Light Touch because I think that is in the best 9 interests of public health. 10 MS. DILLEY: Any other question for Michael 11 before we have -- if there is, I'd also like other 12 panel members to come up. So Scott, Lars-Erik and 13 Mike, come on up. Justine. 14 (No response.) 15 Q&A Session -- Abby Dilley 16 MS. DILLEY: Okay. So as they're getting 17 situated, we had one via e-mail for Lars-Erik. So 18 when you're seated. 19 So this is from Joanna Cohen, Lars-Erik. 20 "Yesterday Professor Carpenter --" in the IOM, his 21 presentation on the IOM report -- "presented a 22 letter from you to the IOM that indicated that</p>	<p style="text-align: right;">Page 168</p> <p>1 (No response.) 2 MS. DILLEY: Okay. Any questions from the 3 audience? Otherwise, we have other e-mails. 4 Introduce yourself, please. 5 MR. DELMAN: Farrell Delman, TMA. 6 Great job, Michael. I thought that was a 7 super address. And you were up at the SRNT, and we 8 chatted a little bit about the MHRA and Light Touch 9 regulation proposal that we heard from Mike Jarvis, 10 I think it was who pitched it. 11 I'm still trying to get my hands around how 12 CTP's going to address the population risk issues 13 associated with the MRTTP products. And certainly 14 in the context of Light Touch regulation, that 15 seems to create an interesting puzzle because 16 population risk, as we well know in the public 17 health standard, has yet really to be defined in 18 terms of how you get your hands around it, in terms 19 of how you design a model to capture it. 20 Since you're the innovation guru on this 21 panel, I thought maybe you could kick it off, and 22 others on the panel could comment on how if you</p>

<p style="text-align: right;">Page 169</p> <p>1 were the director of CTP, what would you be doing 2 to get your hands around the population risk issue 3 and all of its potential forms -- in fact, we heard 4 Neal Benowitz raise yet another one at the SNRT of, 5 gee, look at all those e-cigarette smokers blowing 6 vapor. Might that not increase something among 7 non-consumers? 8 I mean, there are so many potential ways of 9 framing the population risk issue. How would you 10 as an innovator frame it? And then if anybody else 11 cares to comment. 12 MS. DILLEY: Third-party governance on that. 13 MR. DELMAN: Yes. 14 DR. HUFFORD: So I shudder to think of 15 myself in Mitch Zeller's position. I don't envy 16 the job he has in front of him. From a population 17 risk perspective, there's certainly, I think, some 18 outstanding academic minds that can apply their 19 knowledge and resources to research on that 20 question. What concerns me -- and it's why I 21 showed the Voltaire quote, that the perfect is the 22 enemy of the good -- if we wait until all of the</p>	<p style="text-align: right;">Page 171</p> <p>1 funder typically has final say on research, agenda 2 setting, study design, conduct analysis, and the 3 ability to publish. 4 "Can the speakers comment on this model 5 relative to the criteria discussed by Joanna Cohen 6 on day 1, which included freedom to publish 7 findings, even if negative, and protections against 8 conflict of interest?" 9 DR. WALKER: Let me start by saying we 10 talked about third-party governance. I mentioned 11 the FDA at least in my talk. I really believe that 12 the agency has the governance structure and the 13 governance elements. But we didn't talk much about 14 the TPSAC, which also has an important role to play 15 in third-party governance. It's an independent 16 third party. It helps the FDA with modified-risk 17 applications. It could be used to address some of 18 the scientific standards and some of the 19 methodologies that we need to address. 20 There's no reason we can't have TPSAC 21 meetings over the next 6 to 12 months on some of 22 these critical topics to bring together thought</p>
<p style="text-align: right;">Page 170</p> <p>1 issues are perfectly articulated, that I fear is a 2 recipe, whether through third-party governance or 3 not, for the field to move forward. 4 These are extraordinarily important issues. 5 I think the extent to which you're pursuing a 6 product, where nicotine's profile on health and 7 health risks is so well established, that public 8 health good is likely facilitated most by enabling 9 those products to move forward, with combustible 10 products, I think, probably having a very different 11 threshold for evidence to be approved as a 12 modified-risk tobacco product. And I think there's 13 both science and history to kind of justify that 14 particular position. 15 MS. DILLEY: Okay. I am going with another 16 e-mail question. 17 "Many of the speakers talked about not 18 needing a third-party governance model because 19 they're already working with third parties, 20 including CROs. But typical contractual agreements 21 do not provide complete independence in the way 22 that was discussed on day 1. For example, the</p>	<p style="text-align: right;">Page 172</p> <p>1 from industry, academia, public health, the whole 2 element of people to sit down and say, okay, how 3 would you develop criteria around initiation? How 4 do you address the issues of cessation, special 5 populations? 6 So I think we think there's an increased 7 need for ongoing dialogue, but there are 8 mechanisms. There are things in place that have 9 not necessarily been used to their fullest to 10 articulate how we proceed forward. 11 I would agree with some of the comments 12 earlier that we need to move forward. There's an 13 amazing amount of innovation that's been occurring 14 in the tobacco space over the last three to five 15 years, and the innovation needs to continue. But I 16 would also caution that when we do innovation, we 17 make sure that the pre-market assessment is 18 sufficient in terms of scope of science. We make 19 sure we understand risks upfront, to the degree we 20 can, and then we monitor those risks going forward 21 for these new products. 22 So I think there's a balance between rush to</p>

<p style="text-align: right;">Page 173</p> <p>1 market and good science. I think there's a need 2 for pre-market evaluation of these products in the 3 right kind of context, and then post-market 4 surveillance.</p> <p>5 MS. DILLEY: Anybody else want to respond to 6 that question?</p> <p>7 I guess I would have a follow-up question 8 just in terms of, Michael, using your quote about 9 "As in manufacture, so in science, retooling is an 10 extravagance to be reserved for the occasion that 11 demands it." I hear this tension from different 12 comments on innovation, of public health standard, 13 and transparency of data, and independence of 14 research, conflict of interest.</p> <p>15 Can you address that constellation of issues 16 and whether a role for third-party governance does 17 play a role, or it does demand something different, 18 radically different?</p> <p>19 Michael or anyone. I just used your quote, 20 Michael. I liked the quote.</p> <p>21 DR. WALKER: Can you maybe get a more 22 specific question?</p>	<p style="text-align: right;">Page 175</p> <p>1 independent? Yes, I think you can because in those 2 instances, it's very clear what should be done. 3 The standards are very defined, and so there could 4 be no discussion of how the work should be done.</p> <p>5 I think it's more important to use 6 independent bodies in areas without such clear 7 standards also for setting research priorities 8 because there could be bias in which areas you 9 focus on, which areas you don't look at. And so 10 from a broader perspective, I think there you need 11 more independence.</p> <p>12 MS. DILLEY: Any other comments?</p> <p>13 DR. GRAFF: So I just wanted to follow up a 14 little bit with that. With regard to contracting 15 of clinical studies, there is a great deal of 16 independence built into the Code of Federal 17 Regulations currently with regard to principal 18 investigators that are involved in those studies. 19 For example, at any time, a principal investigator 20 can stop the study if he feels that it's necessary.</p> <p>21 So I've heard this bit about the 22 independence of depending upon where the money is</p>
<p style="text-align: right;">Page 174</p> <p>1 MS. DILLEY: Yes. So I think Michael's 2 quote was in reference to using a different 3 regulatory process, so expediting review or some 4 other things. The specifics on this workshop is 5 around third-party governance, so in terms of 6 looking at Joanna's criteria that she laid out and 7 some other kinds of things, does it take a 8 different approach to access to data -- I mean, I 9 hear confidential business information is 10 imperative because that drives innovation, but then 11 there's also the public health standard. And this 12 is a very different area for product development 13 and review and approval.</p> <p>14 So does that, too, require very different 15 approaches, and can third-party governance play 16 that role, and how?</p> <p>17 DR. RUTQVIST: I think one should apply 18 different standards, depending on what type of 19 research it is. In areas where methodologies are 20 very defined, very clear, let's say in the clinical 21 trials, can you use a paid contractor to do that 22 research, a contractor who is by definition not</p>	<p style="text-align: right;">Page 176</p> <p>1 coming from, and I think we really have to think in 2 terms of what independence is already built into 3 the system as well. It's not a completely 4 non-independent system just because I'm taking 5 money from a pharmaceutical company or a tobacco 6 company, depending upon where the money is coming 7 from.</p> <p>8 MS. DILLEY: Other comments?</p> <p>9 DR. WALKER: Yes, let me just clarify a 10 couple perspectives. I think we talked about in 11 our discussion contract research being done in a 12 sort of independent manner. I agree with the 13 comments that Don made about nothing is completely 14 independent and free from bias, which is why you 15 need vigilance. But I would point out to you that 16 we have, within the agency and within the TPSAC, 17 and within the other processes of the agency uses, 18 a tremendous amount of surveillance and vigilance 19 about the industry research.</p> <p>20 I would point out three things that I think 21 about. One is people, one is process, and the 22 other is power. So when I think about what the</p>

<p style="text-align: right;">Page 177</p> <p>1 agency can do in the area of this research to help 2 put standards in place, to help monitor research, 3 study conduct, it occurs to me that they have 4 people that have highly specialized skillsets. 5 From the center director all the way down to office 6 of science, communication, policy, you've got 7 people who've worked in the field of tobacco 8 control, tobacco research, for decades. You have 9 people who understand the problems and the history. 10 You have people who have science degrees. You've 11 got a lot of the elements that need to be in place 12 so that you can monitor and conduct research in a 13 very transparent and a very ethical way. 14 In terms of processes, the model we're 15 talking about, the contract research model, 16 although not perfect in all circumstances is a very 17 good model for which I think we can form the basis 18 for much of the research we do going forward. 19 There is a fair degree of independence of 20 the contract research organization from the 21 sponsor. They do site selection, study monitoring. 22 They do all the things that you would normally</p>	<p style="text-align: right;">Page 179</p> <p>1 conduct in place today. 2 MS. DILLEY: So questions, Corinne. 3 DR. HUSTEN: Corinne Husten, FDA. I just 4 wanted to ask the panel, yesterday, one of the 5 models that was put forward by Dr. Cohen was this 6 idea that the independent organization was really 7 more of an organization to put out for open sort of 8 competitive proposals to do research to answer the 9 specific question. And I guess I'd like to hear 10 what the panelists see as sort of the disadvantages 11 of that type of approach, where instead of directly 12 contracting, it's a more open process where there's 13 an independent review of proposals to assess the 14 study strengths. 15 So anyway, I'd just be interested in hearing 16 specific -- because that was a specific sort of 17 model that was put forward, and I haven't really 18 heard anyone talk about that model. 19 MS. DILLEY: Any response? I think everyone 20 was here for that presentation. Michael? 21 DR. HUFFORD: I would just note, wearing my 22 hat from my days helping to work in and grow a</p>
<p style="text-align: right;">Page 178</p> <p>1 associate with independence and freedom. They 2 select investigators. And I can tell you, having 3 worked in industry for almost 20 years, when you 4 work under FDA regulation and when you sponsor 5 studies, you're always mindful of everything you do 6 and how it might run counter to the FDA's 7 perspective on your study. You don't want bias in 8 your study because you know at the end of the day, 9 you go before a review committee and before the 10 agency, and you've got problems. 11 So I think there's people, there's a 12 process, and, finally, we should not forget that 13 the FDA has the regulatory authority. It has the 14 power to set standards, to make decisions. And we 15 may agree or disagree at the end of the day, but 16 the agency is the regulatory body. 17 So when I think about all the elements that 18 FDA has, I think we should really consider there's 19 tools we can use today, we should use. We can 20 perfect them over time if they prove insufficient. 21 We can modify them. But we have constructs for 22 third-party governance and effective clinical study</p>	<p style="text-align: right;">Page 180</p> <p>1 number of contract research organizations and 2 sitting on innumerable project teams, both on the 3 sponsor and on the vendor side, I think it holds 4 tremendous intellectual appeal. 5 It concerns me a little bit of sort of, one, 6 the mechanics of how it would work and whether it 7 would potentially slow research considerably, is a 8 real concern of mine. Do the projects get awarded 9 to the lowest bidder among all competitive 10 proposals? 11 If a company has other pharmaceutical and 12 biotech clients, have medical directors that are on 13 the phone with them every single day helping make 14 decisions about how research is executed, if these 15 products are sort of given to a third-party 16 organization and kind of, then, the research is 17 farmed out -- I just worry about the logistics of a 18 little bit of how exactly is that going to work at 19 the project team level? How is it going to compete 20 with other pharmaceutical industry projects? 21 Especially around some of the sources of 22 expertise. You know, again, it's just been my</p>

<p style="text-align: right;">Page 181</p> <p>1 experience, kind of both being a medical director 2 or working with them closely on the collaborative 3 side, their role is so central in the drug 4 development model, in the CRO model, I haven't 5 quite gotten my head around how that would work 6 with applied to these products when the source of 7 expertise resides at the funding company, and how 8 some of those decisions would be made or who even 9 is going to make them.</p> <p>10 I think a lot of CROs would not have the 11 expertise would not have the expertise to make 12 those decisions when it comes to modified-risk 13 tobacco products because they just don't have the 14 relevant technical expertise.</p> <p>15 DR. HUSTEN: Just to clarify, I wasn't 16 saying that the organization would be making any 17 decisions. It's just purely a way to have an 18 independent review of the research design and 19 proposal, and to have -- maybe break the link a 20 little bit between the funding and the actual 21 research in the sense that the funding doesn't 22 depend on -- it's purely on the expertise in the</p>	<p style="text-align: right;">Page 183</p> <p>1 the issue of consumer perception research, so my 2 comment was of a more general nature.</p> <p>3 MS. DILLEY: I just thought the mechanism of 4 putting out design elements were -- it was part of 5 some of your work.</p> <p>6 DR. RUTQVIST: Well, it's what we did in the 7 clinical trials, but I think what Corinne is 8 referring to is something different</p> <p>9 MS. DILLEY: Mike?</p> <p>10 DR. OGDEN: I think that model might have 11 some merit if you -- in some areas of MRTTP 12 research, as I carved them out in my presentation, 13 you talk about basic tool development versus the 14 sponsor's obligation to develop science specific to 15 a product application, and then post-market 16 surveillance.</p> <p>17 I think to your question, Corinne, in the 18 first instance of developing basic tools to answer 19 fundamental questions, that seems entirely 20 appropriate to me. And I think that's the way you 21 framed your follow-up question. If you want to 22 answer the question about consumer perception, you</p>
<p style="text-align: right;">Page 182</p> <p>1 study design that they submitted.</p> <p>2 So, for example, if you had a modified-risk 3 tobacco product application and you needed three or 4 four different types of studies, and one was around 5 consumer perception, that particular interest would 6 be put up for a competitive proposal for people to 7 come in who have expertise in consumer perception 8 to propose how they would look at that issue and 9 design a study to give results.</p> <p>10 Again, it's just potentially a way to 11 address what we were hearing, was skepticism about 12 the credibility of the research. I was just 13 concerned about what you saw as the major flaws of 14 that type of a potential design.</p> <p>15 MS. DILLEY: Lars-Erik, I thought you spoke 16 to that. I thought you spoke to that a little bit 17 in terms of contracting out some of the --</p> <p>18 DR. HUSTEN: I just want to clarify, it 19 wasn't a decision-making body. It was purely to 20 fund the -- peer review or to have an expert panel 21 review the research proposals.</p> <p>22 DR. RUTQVIST: I didn't particularly address</p>	<p style="text-align: right;">Page 184</p> <p>1 would seek competitive proposals or protocols on 2 how to do that.</p> <p>3 I think if you're in the second area, where 4 it's product specific, I then would share Michael's 5 concern. I think in my view, it falls to the 6 sponsor to decide, in consultation with the agency, 7 as to what an appropriate protocol would be. And 8 if you went then at that point to go to some 9 third-party structure and started shopping around 10 different protocols, that could take quite a bit of 11 time, again, without any a priori knowledge of 12 which protocols might deliver more robust results, 13 et cetera.</p> <p>14 So I think it could be useful in some areas, 15 but I think in the area of sponsor-specific work, I 16 don't think that would work. But in basic tool 17 development, perhaps even in post-market 18 surveillance, there might be some merit to that.</p> <p>19 MS. DILLEY: Matt, and then we had some 20 other e-mail questions.</p> <p>21 MR. MYERS: This is to Don. In trying to 22 figure out the role of organizations like yours</p>

<p style="text-align: right;">Page 185</p> <p>1 versus some sort of independent third party, I was 2 trying to get a sense of when a company comes to 3 you, the relative role of your organization versus 4 their organization; and, A, developing the study 5 design; and, B, even more broadly, deciding what it 6 is that needs to be studied.</p> <p>7 DR. GRAFF: Sure. So it really depends on 8 the company that comes to us. So we have some 9 sponsors, both in the pharmaceutical industry and 10 the tobacco industry, that come to us with fairly 11 complete study protocols and designs, and they have 12 a really good understanding based on what they 13 might have done in the past so that they have a 14 really good idea of the best design that they have 15 in mind for this particular study to answer the 16 questions that they want to have.</p> <p>17 On the other end of the spectrum, we 18 sometimes have -- again both in pharmaceutical and 19 tobacco sponsors -- people who come to us with 20 really no idea. They have a basic idea of what it 21 is that they want to try to find out. They may not 22 have a specific objective yet at that point, but</p>	<p style="text-align: right;">Page 187</p> <p>1 tobacco industry.</p> <p>2 MR. MYERS: So as your organization does its 3 work then, do you take a look at -- if somebody 4 comes to you with a study design and say to them, 5 well, that's not really going to tell us whether or 6 not the product is safe, or in the case of tobacco 7 where it's a complex product, if the change you 8 made, we can measure whether or not you've 9 effectively made the change. But it's not going to 10 tell us whether or not the product causes less 11 disease.</p> <p>12 DR. GRAFF: Right. And so I think where 13 we're at right now, at least with Celerion, we're 14 not to the point yet that we're evaluating disease. 15 I think we're really good at the exposure part of 16 that. And so that's probably one of the gaps in 17 the company that I work for right now is, okay, we 18 had a really good idea of the exposure of these 19 products. We can evaluate them differently, dual 20 use, single use, cessation, the whole -- we've got 21 a plan for all of that.</p> <p>22 It's now taking it to the next step, and</p>
<p style="text-align: right;">Page 186</p> <p>1 they want to evaluate a product. So how do we best 2 go about that? And there's really everything in 3 between that we might see as well.</p> <p>4 After we talked at the break, one of the 5 things that I thought about was, currently, we 6 probably write and help design I'm going to guess, 7 50 percent or more of the ideas that come to us 8 from the tobacco industry. On the pharmaceutical 9 side, we really have input on writing the protocols 10 on about 20 percent.</p> <p>11 Now, that's not to say we don't have some 12 input because every study that comes to us, if 13 we're going to conduct the study, we have an 14 operational review so that the clinic knows -- can 15 handle the logistics. And if we do the backend 16 data analysis and data interpretation, we have our 17 clinical pharmacologist and statisticians review as 18 well. So we do have input in those areas.</p> <p>19 Now, in some cases our input is taken and 20 politely set aside. In other cases, it's been 21 incorporated into the designs of the studies. And, 22 again, this is for both the pharmaceutical and</p>	<p style="text-align: right;">Page 188</p> <p>1 that is, evaluating these things long term and how 2 are we going to evaluate the health risks of those. 3 Those types of studies are ongoing, but they're 4 really sort of in their infancy, in my opinion.</p> <p>5 MS. DILLEY: Thank you.</p> <p>6 Justine, you wanted to comment?</p> <p>7 MR. APELBERG: Abby, can I just make a quick 8 comment there? What kind of -- sort of chemical 9 smell --</p> <p>10 (Discussion off the record.)</p> <p>11 MS. DILLEY: Justine, sorry. Go ahead.</p> <p>12 DR. WILLIAMSON: I'm relatively new to my 13 role of -- I'm head of biosciences, so I'll sort of 14 speak to as much detail as I know. But we 15 have -- and we're about to publish on a reduced 16 toxicant combustible product clinical study. We'll 17 be publishing the results of this next week. And 18 when it came to designing the protocol, we're going 19 a little bit back in time, yet we were very much 20 consulting with literally as many people as we 21 could, because this is an area that was new to us, 22 so we were talking to external experts. We were</p>

<p style="text-align: right;">Page 189</p> <p>1 speaking and listening to the CROs to get their 2 expertise. 3 So I think it's a learning process. We took 4 the learnings from that. We've got the second 5 clinical study data now in lockdown, and I think 6 it's about -- we put our protocols out there. 7 We're putting our data out there. We may make 8 mistakes, but I think it's just about 9 keeping -- putting the data out there, and let all 10 of us keep looking at it and seeing what are the 11 right protocols for us all to be using. 12 MS. DILLEY: Okay. I have an e-mail 13 question. This is from Mark Parascandola, and it's 14 to you, Mike. 15 "So presumably, RJR is already conducting 16 some research on tobacco products. Would you 17 consider making information about all ongoing 18 research projects publicly available? For example, 19 this could be done in a format similar to 20 clinicaltrials.gov, providing summary information 21 about study aims, methods and results." 22 DR. OGDEN: I think the question</p>	<p style="text-align: right;">Page 191</p> <p>1 Tobacco. I think I've been able to clarify the 2 question I failed to articulate yesterday, but I 3 think some of the speakers today have actually 4 answered it. But nonetheless, the question I 5 wanted to ask was, would FDA approval of one or 6 more third-party governance entities increase the 7 production, or the dissemination, or the 8 credibility of research to support modified-risk 9 tobacco product applications? 10 MS. DILLEY: So you'd like to hear the panel 11 member -- 12 MR. MOYNIHAN: I'd like to hear each person 13 answer that in a simple, not yes or no, but as 14 close as possible. 15 MS. DILLEY: Anybody want to start? Scott? 16 DR. OGDEN: What was the question? 17 MR. MOYNIHAN: The question is, I'm 18 concerned about sort of a fairly specific answer in 19 response to Recommendation 10, really, which I 20 think some of you have answered. But so the 21 question is, would FDA approval of one or more 22 third-party governance entities increase</p>
<p style="text-align: right;">Page 190</p> <p>1 was -- well, based on current research, my 2 understanding is all of our clinical trial research 3 is registered at clinicaltrials.gov. That was not 4 true going back 8 or 10 years, but the information 5 is publicly available of the types of studies we've 6 done. Certainly, information on those studies is 7 available to FDA as being produced through the 8 health documents discovery, et cetera. 9 So I think with our view to conforming with 10 societal expectations, I think, yes, we would 11 entertain that notion of -- to the extent we're not 12 doing it now, we would entertain the notion of 13 making the visibility of those trials to the 14 appropriate level. Our intention is to publish and 15 present those results in due course. As many have 16 mentioned, there's some barriers to doing that in 17 an expeditious way with industry funding, but 18 certainly, all of those data then become 19 transparent, fully transparent to FDA. 20 MS. DILLEY: Questions from the audience, or 21 else I'll go back to the e-mails? 22 MR. MOYNIHAN: Michael Moynihan, Goodrich</p>	<p style="text-align: right;">Page 192</p> <p>1 production, dissemination, or credibility of 2 research aimed at supporting an application for a 3 modified-risk tobacco product? 4 MS. DILLEY: So specifically an application. 5 So I think some people addressed those in their 6 comments, but he'd like you to respond to that. It 7 could be, it depends, yes, no. 8 DR. WALKER: Maybe, maybe not. I think it 9 depends on the framework that you're talking about. 10 It depends on the questions you're asking. I think 11 it depends on whether the research is of a general 12 nature or if it's product specific. 13 MR. MOYNIHAN: Only product specific. 14 MS. DILLEY: Only product specific for MRTPs 15 in particular. 16 DR. WALKER: So our perspective is that that 17 process needs to be gone through the FDA. We think 18 that the FDA has and can acquire the requisite 19 knowledge and expertise to make those kinds of 20 determinations in a pre-market setting. 21 Do I think a third party on top of the FDA 22 would be more efficient? The answer is probably</p>

<p style="text-align: right;">Page 193</p> <p>1 not. I think it would be less efficient. It 2 really depends, though, on how it's structured, the 3 questions that are being asked. 4 So I guess that's my maybe, maybe not. 5 You'd have to be very specific about the kind of 6 structure, the kinds of considerations, and the 7 level of authority that you give to such a 8 governance body before I could really answer the 9 question. 10 MS. DILLEY: Justine? 11 DR. WILLIAMSON: I think, in general, if we 12 have a defined structure, if we have defined tools, 13 it will make everyone's life easier because we will 14 know then where we're trying to get to. And I 15 think probably because there is uncertainty, 16 especially around some of these tools, around abuse 17 liability and where we go with those, that is at 18 the moment probably slowing things down -- once 19 that's in place and is agreed by everyone, then I 20 think potentially, yes, things could increase in 21 speed. 22 MS. DILLEY: Lars-Erik?</p>	<p style="text-align: right;">Page 195</p> <p>1 no model for that, and it would be difficult to see 2 how it would add value. 3 Now, that's not to say that's true in all 4 cases, but, specifically, I think your question, 5 Michael, about specific product pre-market 6 research, our position is that that would slow 7 things down and would not be in the best interests 8 of the process or moving the modified-risk tobacco 9 product to market in a timely way. 10 MS. DILLEY: Michael Hufford. 11 DR. HUFFORD: So my one word answer would be 12 maybe, and, Michael, to reiterate something that I 13 said at SRNT last week, I think investors live on a 14 teeter-totter between fear and greed. And 15 regulatory uncertainty is an enormous part of the 16 fear equation here that freezes capital, which is 17 frozen energy, I think, from coming into the space 18 and funding more innovations to come forward. 19 I think it's -- the agency may be completely 20 aware of this. I just don't know, that lack of 21 clear action is interpreted by many folks as a 22 concern, as a barrier, as a reason not to move</p>
<p style="text-align: right;">Page 194</p> <p>1 DR. RUTQVIST: The definition of an MRTP is 2 very complex and requires many different types of 3 studies. Would it increase credibility if these 4 studies have oversight from third parties or 5 involve third parties? Yes, I think it would. 6 Would a sort of overall third party that 7 oversees the whole process add anything to this? 8 I'm not so sure. 9 DR. OGDEN: I think I would echo many of the 10 comments I've heard, just to summarize some of 11 those. I mean, I share -- we share Jeff's concern 12 about the notion of the word "governance" and what 13 that means, and does that -- it appears to imply 14 relinquishing of either the rights or the 15 responsibility of either the sponsoring industry, 16 company, or the agency. That's problematic. 17 If governance were to be imagined as TPSAC 18 review, which is specifically authorized in the 19 act, no, not a problem. As it goes beyond that, I 20 think you have to be -- we would approach that with 21 caution. And at this point where we sit at the 22 table is that that's not what's required. There's</p>	<p style="text-align: right;">Page 196</p> <p>1 forward. So I would see any clear action that 2 clearly articulates what the path forward is, I 3 think, will do a service to bringing innovation and 4 capital into the space. 5 MS. DILLEY: Donald? 6 DR. GRAFF: So I'm going to use two words, 7 and I would say not necessarily. So my viewpoint 8 is again from a very operational level, is having 9 the framework in place or at least some idea of 10 what it's going to take to get a product approved, 11 with some specifics behind that. And so start 12 there, and then start working your way back and 13 determine whether or not a third-party governance 14 structure is actually required. So instead of 15 okay, let's define this structure and then figure 16 out how it's going to work, start from the end and 17 sort of work your way back. 18 MS. DILLEY: Scott? 19 MR. BALLIN: Something I said this morning 20 about the bureaucracies, we don't want to create 21 exorbitant bureaucracies that actually have 22 negative effects on trying to accomplish a public</p>

<p style="text-align: right;">Page 197</p> <p>1 health goal. That happens all the time.</p> <p>2 So I would say it depends on how it's done,</p> <p>3 but we don't want to sacrifice progress by creating</p> <p>4 bureaucracies, but we also want to make sure that</p> <p>5 the system works properly and there is proper</p> <p>6 oversight. Now, whether that's done by FDA and it</p> <p>7 needs to talk to people or saying we need some</p> <p>8 additional advice on this, I don't know how that</p> <p>9 could be done, but it's an alternative instead of</p> <p>10 setting up something that's too complex.</p> <p>11 MS. DILLEY: I have an e-mail question.</p> <p>12 "This is a follow-up to Dr. Cohen's e-mail</p> <p>13 question. Both Mike Ogden and Justine Williamson</p> <p>14 mentioned that potential need for third-party</p> <p>15 governance regarding vulnerable populations. I</p> <p>16 think this is in the research tools category, e.g.</p> <p>17 adolescents. What are your thoughts regarding the</p> <p>18 most appropriate governance structure to conduct</p> <p>19 this type of research?"</p> <p>20 Justine, do you want to start on that?</p> <p>21 DR. OGDEN: Well, I touched on some of this</p> <p>22 in my prepared comments earlier. I mean, I see</p>	<p style="text-align: right;">Page 199</p> <p>1 standstill unless we find some third solution. And</p> <p>2 under those scenarios, if we cannot make it work</p> <p>3 directly with the agency, then we would explore</p> <p>4 other options, and a governance model might be</p> <p>5 appropriate there.</p> <p>6 MS. DILLEY: Justine?</p> <p>7 DR. WILLIAMSON: Similar lines.</p> <p>8 MS. DILLEY: I think this is a follow-on</p> <p>9 question that's very similar, that you indicated</p> <p>10 "that BAT has expertise in risk perception and</p> <p>11 post-marketing surveillance. Thus, do you feel</p> <p>12 that BAT could sponsor and conduct this type of</p> <p>13 research in support of MRTP applications? And if</p> <p>14 third-party governance is needed for this type of</p> <p>15 research, what type of governance model would you</p> <p>16 recommend?"</p> <p>17 DR. WILLIAMSON: So maybe slide was a little</p> <p>18 misleading. I can't remember what was in the</p> <p>19 banner, but these were areas that we are developing</p> <p>20 in. So right now, no, we do not have enough</p> <p>21 expertise in these areas. So that's why we are</p> <p>22 looking to dialogue on these areas and speaking to</p>
<p style="text-align: right;">Page 198</p> <p>1 that as an area that has potential concerns. I</p> <p>2 mean, we're aware of what those concerns are. I</p> <p>3 think if that type of research is required for a</p> <p>4 modified-risk tobacco product application, and it</p> <p>5 appears that it is, then our view at this point</p> <p>6 would not waiver, that that is the responsibility</p> <p>7 of the sponsoring company to conduct that research.</p> <p>8 We have made it clear with FDA, going back</p> <p>9 two years now at least, by letters, by sending</p> <p>10 draft protocols, and by asking for clarification as</p> <p>11 to specifically on this point. Our position is</p> <p>12 that we have tools that are appropriate and we</p> <p>13 believe applicable in that space. But we will not</p> <p>14 conduct those types of research unless or until FDA</p> <p>15 is explicitly clear with us that that information</p> <p>16 is required and that they -- at least we have a</p> <p>17 meeting and we agree to the protocol.</p> <p>18 So under those circumstances, I would say at</p> <p>19 this point, we have not done that research yet, but</p> <p>20 I think that it's possible that we would. If that</p> <p>21 becomes a necessary component and we cannot get</p> <p>22 that direction from FDA, then I think we're at a</p>	<p style="text-align: right;">Page 200</p> <p>1 the correct experts in the field to develop the</p> <p>2 expertise in house.</p> <p>3 MS. DILLEY: And there was another question</p> <p>4 to you, Justine, on the same e-mail.</p> <p>5 "On your presentation, you indicated that in</p> <p>6 the future, you would consider partnerships with</p> <p>7 NIH. Could you please elaborate on this?"</p> <p>8 DR. WILLIAMSON: I think --</p> <p>9 MS. DILLEY: What would an ideal partnership</p> <p>10 look like, part of that.</p> <p>11 DR. WILLIAMSON: So, yes. I mean, our</p> <p>12 understanding is that the TCORS and the NIH-type</p> <p>13 funding don't exclude the industry. But what we</p> <p>14 would sort of -- what we were saying in that</p> <p>15 statement there is that for those research partners</p> <p>16 who are looking to take on that funding, and they</p> <p>17 need some additional support, that we may be able</p> <p>18 to give them.</p> <p>19 So like any expertise we have, maybe our</p> <p>20 analytical services -- one example that institutes</p> <p>21 have been coming to speak to us about is our</p> <p>22 experience around whole smoke exposure systems. We</p>

<p style="text-align: right;">Page 201</p> <p>1 are doing a lot of work in that area, and a lot of 2 parties are interested in working with us on that. 3 But because of their restrictions via taking 4 funding, they're unable to talk to us about that. 5 So what we would say is if those guys were 6 going to want to do work in that area, then maybe 7 they want to go down that route, and we could then 8 potentially offer advice, support, help through 9 those more transparent and organized funding 10 mechanisms. 11 MS. DILLEY: Other questions from the 12 audience? 13 (No response.) 14 MS. DILLEY: I've got another question from 15 Mark Parascandola. 16 "The tobacco industry presenters mentioned 17 or described ongoing research efforts around 18 tobacco products and harm reduction. Some are 19 publishing papers and making presentations on their 20 science. To be fully transparent, the companies 21 could make detailed information publicly available 22 about all studies they conduct, including</p>	<p style="text-align: right;">Page 203</p> <p>1 our plans. As we would anticipate starting 2 clinical trials, we would meet with the agency 3 before starting the trials to make sure the 4 protocol and the methodology is correct, meet with 5 consultants, meet with contract research 6 organizations. 7 So our efforts right now are focused within 8 the regulatory framework, and we do not have at 9 this point in time a mechanism to talk about, 10 particularly, pre-market studies. There's 11 certainly particular issues around competitively 12 sensitive information where you wouldn't want to 13 necessarily tell everyone what you were doing 14 because your competitors would sort of be alerted 15 to, well, gee, they're working on this new product. 16 Maybe I should work on the product, too. 17 So there's some really practical limitations 18 to early disclosure of research. I think we're 19 going to work through those. I think we're still 20 working through when it's appropriate to list on 21 clinicaltrials.gov. And I think at the present 22 time, as we get ready to conduct large clinical</p>
<p style="text-align: right;">Page 202</p> <p>1 disclosing study aims and methods before work is 2 started and making all results and data public. 3 Can each of the presenters describe their 4 own company's plans for scientific data and 5 information sharing?" 6 DR. WILLIAMSON: And I probably spoke to 7 this one a little bit before. As I said, we're 8 publishing next week on our reduced toxicant 9 combustible clinical study that we ran a couple of 10 years ago now. Now, that's the results that we 11 were publishing. We're already published the 12 methodology. We've already published on the 13 technologies included in that product. 14 So that's very much the approach we're 15 taking, is just to publish as much as we can along 16 the road. 17 MS. DILLEY: Other comments, Jeff? 18 DR. WALKER: From our perspective, we are 19 being very transparent, very forward with the 20 agency with regard to our studies. When we want to 21 think about proceeding forward in a new area with a 22 new product, we meet with the agency and tell them</p>	<p style="text-align: right;">Page 204</p> <p>1 studies, we would want to make that information 2 available, but in an appropriate timeframe, in the 3 appropriate venue. 4 MS. DILLEY: Lars-Erik? 5 DR. RUTQVIST: When it comes to clinical 6 trials, we obviously follow the pharma model and 7 register the trials at approved clinical trial 8 sites. Otherwise, when it comes to other types of 9 research within academia, there is no sort of 10 accepted way of disclosing that type of 11 information. So we obviously disclose it to the 12 FDA, but apart from that, we haven't really 13 considered using any model of our own that is 14 different from what you would normally do in 15 academia. 16 MS. DILLEY: Yes. And I think this question 17 is less specific to FDA because they don't disclose 18 the information publicly, but it's the broader, the 19 public disclosure. 20 DR. RUTQVIST: Yes. 21 MS. DILLEY: Michael? 22 DR. OGDEN: Very similar to the comments</p>

<p style="text-align: right;">Page 205</p> <p>1 previously, I think there's appropriate ways to 2 disclose research, and then there's perhaps 3 inappropriate ways to disclose research. And in 4 this vein, I'm talking about the competitive nature 5 of things that Jeff spoke about. And that extends 6 not just to the fact that you're working on a 7 product, but how you're evaluating it. 8 We have SOPs in place for all preclinical 9 chemistry and in vitro and in vivo toxicology 10 testing. We have protocols that we use for 11 clinical trials. To simply make that publicly 12 available divests us of a significant amount of 13 information that others would like to have. 14 We know there's been a mad scramble around 15 the world for a couple of years developing 16 laboratory capacity and methods for harmful and 17 potentially harmful constituent testing. If we 18 were to put all of our SOPs out there, then 19 contract labs would pick that up, and there would 20 be competition there that may not always be in 21 everyone's best interest. 22 So I think that the timeliness, certainly</p>	<p style="text-align: right;">Page 207</p> <p>1 interesting model, and I was interested in that 2 because as I heard the presentation and, in fact, I 3 asked a clarifying question, he described more than 4 a dozen studies obviously over probably that many 5 years at least, and then additional information 6 comes to light. 7 So I think once you've done clinical work in 8 a pre-market mode, a product hopefully in a future 9 world gets clearance. It goes to market. Other 10 studies, I mean, the sponsor continues to do 11 research. Others pick up the product and do their 12 own research, and now you build a larger body of 13 data. 14 Particularly if findings start to point in 15 different directions, I think at that point, it is 16 an interesting model to consider, okay, let's bring 17 all of this together and try to find out what the 18 real answer. And maybe it's simply a difference in 19 methodology or statistical methods or whatever, but 20 I think in that instance, that is an interesting 21 model. 22 MS. DILLEY: We'll finish out the rest of</p>
<p style="text-align: right;">Page 206</p> <p>1 the right way to present that information. We do 2 publish. We do present. But there's a lag there 3 because of just the fact that you're investigating 4 a certain type of product. But if you look back 5 over the course of the development of a premier 6 cigarette, for example, culminated in a nearly 7 500-page book that laid out all of that 8 information, again, it's not raw data, but then I'd 9 fall back to where my previous colleagues were. In 10 an FDA context, all of those raw data, then those 11 are perfectly transparent and available to the FDA, 12 including all SOPs or constructions, and everything 13 else that governs the conduct of that research. 14 MS. DILLEY: I think the Medtronic example 15 and the open-data access project looked at the 16 timing. So your point about timing and pre-market, 17 I think they're trying to figure out timing as 18 well, but also make a commitment upfront to -- I 19 think that's what's Mark's asking is kind of an 20 upfront commitment of publishing that data at some 21 point. 22 DR. OGDEN: Well, I think that's an</p>	<p style="text-align: right;">Page 208</p> <p>1 the panel. Michael, did you want to speak to that 2 issue? 3 DR. HUFFORD: Just that my colleagues and I 4 all come from a world of drug development, so we 5 absolutely intend to proceed down that path, filing 6 everything on clinicaltrials.gov, being completely 7 transparent with the agency, publishing our 8 findings, and certainly take the CTP's lead. If 9 the expectation is to make even raw data publicly 10 available, then we'd follow that lead. 11 MS. DILLEY: Don, you want to add anything? 12 DR. GRAFF: No. 13 (Laughter.) 14 MS. DILLEY: Scott? No. Okay. 15 So we have maybe time for one or two more 16 questions. I'm out of the e-mail questions, so I 17 don't know if there are any more coming. Okay. 18 MR. DELMAN: Farrell Delman, TMA. I'm still 19 suffering something of a disconnect in this whole 20 conversation, based on information that you see 21 regularly. I saw it the first time, I think, when 22 I was at the SRNT meeting four years ago, when</p>

<p style="text-align: right;">Page 209</p> <p>1 Dorothy Hatsukami presented a relative risk 2 continuum. And at one end, we had NRT. At the 3 other end, we had cigarettes. Snus was closer to 4 NRT. E-cigarettes were not on that first chart. 5 They've only kind of joined the chart in more 6 recent presentations. 7 When you look at these categories of tobacco 8 products, there does seem to be a certain sense out 9 there -- maybe it's just intuition, or maybe people 10 have gotten ahold of some epi data from Sweden, or 11 there's an assumption that if you inhale a tobacco 12 product, the combusted tobacco product, it's 13 different than if you don't inhale, like with a 14 cigar. So it might have a different place on the 15 spectrum. That's one observation. 16 Another observation -- and then I'm going to 17 put them together -- is that we're shortly going to 18 be dealing with tobacco products standards, right? 19 And when you look at the TCA timeline, you see that 20 tobacco products standards are likely to be a 21 source of conversation. The docket will be open 22 and so on. And it's certainly also the case, many</p>	<p style="text-align: right;">Page 211</p> <p>1 product's risk levels are, safety issues, but I'd 2 also like to know -- I'd like to see a relative 3 risk continuum that somehow incorporated population 4 risk issues into it as well. 5 That would be something that FDA should want 6 to do itself, through contracting research and 7 getting results from the best experts out there, 8 and that individual companies then might end up 9 having a set of standards and rules for the kind of 10 research that would be appropriate for individual 11 product categories for which they would wish to 12 have a brand in, and present the data to FDA the 13 way we've been talking about it, mostly during this 14 session. 15 So I guess I'm wondering if separating 16 product category from brand makes any sense at all, 17 in light of the TCA timeline. 18 MS. DILLEY: Well, that's a different take, 19 but I think Michael Hufford touched on that, 20 somewhat, in terms of categories of relative -- I 21 guess I would say you're talking about relative 22 risk. But any other comments on that?</p>
<p style="text-align: right;">Page 210</p> <p>1 of us are expecting, deeming regulations, for all 2 tobacco products to be shortly presented at the 3 April deadline or whatever, results in deeming 4 regulations. 5 This is all by way of saying that it seems 6 to me that in these conversations about 7 industry-sponsored research, we're always talking 8 about a brand that companies will be bringing to 9 the table, and historically FDA has operated at the 10 brand level. Companies sponsor something. They 11 bring their data. FDA reviews it. 12 I'm wondering if the panelists could address 13 the question of whether the governance issue could 14 be divided, say, over product categories as one set 15 of issues that FDA may wish to address as a product 16 category, and the brand issue within a product 17 category. 18 For example, it would seem to me that if I 19 were engaged at CTP, I sure would like to have a 20 relative risk continuum. I would like to have some 21 idea, certainly based on the impacts on the 22 consumers themselves, of what the individual</p>	<p style="text-align: right;">Page 212</p> <p>1 DR. RUTQVIST: As you know, there's a lot of 2 documentation on long-term effects of a number of 3 combusted tobacco products, and there is a lot of 4 information on long-term effects of some smokeless 5 products. And I think the best documented product 6 there, as you suggested, is Swedish snus. 7 Now, whether category-specific information 8 at all is interesting to the FDA, I don't know. 9 I'm not a lawyer. But it's my impression that the 10 FDA is obligated to focus on product-specific 11 information. 12 As a scientist in this area, if you have a 13 nicotine or tobacco product that is smokeless, it 14 is likely that the long-term health effect profile 15 of that product is more similar to the ones in that 16 product category that we know about, like snus, 17 rather than smoke products. But that is just 18 conjecture. I mean, you don't know that. 19 It's my impression that the FDA needs 20 product-specific information. I don't know if 21 they're interested in category-specific 22 information.</p>

<p style="text-align: right;">Page 213</p> <p>1 MS. DILLEY: Any other comments on that?</p> <p>2 DR. OGDEN: I agree with Lars-Erik. I think</p> <p>3 at least our experience and expectation is that FDA</p> <p>4 is interested in product-specific information for,</p> <p>5 for example, in modified-risk claim.</p> <p>6 But to answer your question, I think sort of</p> <p>7 categorical differences are probably best not</p> <p>8 handled through the modified-risk pathway, but</p> <p>9 through health warnings. And many, if not all,</p> <p>10 know that Reynolds has filed a citizen's petition</p> <p>11 with FDA, challenging one of the smokeless</p> <p>12 warnings, the one that was highlighted this</p> <p>13 morning, that says smokeless tobacco is not a safe</p> <p>14 alternative cigarette. That's a half truth at</p> <p>15 best.</p> <p>16 So a more appropriate warning label there I</p> <p>17 think would go a long way to carving out that</p> <p>18 categorical difference that virtually everyone</p> <p>19 agrees has been firmly documented over a decade or</p> <p>20 more.</p> <p>21 MS. DILLEY: Any other comments? And we're</p> <p>22 going to wrap up. Don?</p>	<p style="text-align: right;">Page 215</p> <p>1 Concluding Comments</p> <p>2 DR. ASHLEY: I would like to thank</p> <p>3 particularly all the invited speakers who came.</p> <p>4 I'd like to thank those folks who came and</p> <p>5 presented in the open public time. And for</p> <p>6 everybody else who's participated in the workshop,</p> <p>7 those of you who came in person, those of you who</p> <p>8 joined us remotely, and just give you my sincere</p> <p>9 appreciation for that.</p> <p>10 Also, I'd like to thank everyone who</p> <p>11 participated in the questions and answers, and</p> <p>12 asked very good questions, very thoughtful</p> <p>13 questions, and I really appreciate that.</p> <p>14 A couple of things I took out of today's</p> <p>15 discussion were, particularly, areas around the</p> <p>16 challenges of how to address the range of products</p> <p>17 that are made or derive from tobacco. Clearly, it</p> <p>18 presents some significant challenges to FDA and to</p> <p>19 the industry both on how to have a consistent</p> <p>20 process and -- I still want to go back to</p> <p>21 Scott -- how to be consistent and flexible at the</p> <p>22 same time.</p>
<p style="text-align: right;">Page 214</p> <p>1 DR. GRAFF: Just one comment briefly on</p> <p>2 that. So it's my interpretation of the regulation</p> <p>3 that's out there that with one of these</p> <p>4 applications, you're going to have to do a</p> <p>5 substantial amount of comparisons to not only</p> <p>6 products within a category but across categories as</p> <p>7 well. So I think one of the things that's going to</p> <p>8 come out of these per product/per brand</p> <p>9 applications is a great deal of product information</p> <p>10 across -- on a much broader basis.</p> <p>11 So I think indirectly one is going to result</p> <p>12 in the other one. Now, what the FDA decides to do</p> <p>13 with that, that's for them to decide. Maybe that</p> <p>14 goes into product standards. Again, really, that's</p> <p>15 up to them.</p> <p>16 MS. DILLEY: Any other comments?</p> <p>17 (No response.)</p> <p>18 MS. DILLEY: I want to thank the panel</p> <p>19 members again for your time and presentations.</p> <p>20 (Applause.)</p> <p>21 MS. DILLEY: And I will turn it back over to</p> <p>22 David Ashley to wrap it back up.</p>	<p style="text-align: right;">Page 216</p> <p>1 There are also a couple of things that came</p> <p>2 out that were clear differences among the speakers</p> <p>3 today. There were different views on to what</p> <p>4 degree product-specific research should be carried</p> <p>5 out outside the industry versus inside the</p> <p>6 industry. There were some differences of opinion</p> <p>7 on making MRTP-supporting data available to the</p> <p>8 public, whether that should be made available or</p> <p>9 not made available.</p> <p>10 But there were also some common themes that</p> <p>11 came out, particularly on the need for specifics on</p> <p>12 how to conduct studies and what specific studies</p> <p>13 are needed. Clearly, that is a work in progress</p> <p>14 and will continue to be for a while.</p> <p>15 Also, the major challenges around youth and</p> <p>16 other subpopulations, which was highlighted in the</p> <p>17 IOM report, unfortunately, no one stepped up and</p> <p>18 said here's how you solve that problem. It is</p> <p>19 definitely an issue. It will continue to be an</p> <p>20 issue for some time as we work through that, and</p> <p>21 there's clearly a common theme around that.</p> <p>22 As I said at the beginning of day 1, the</p>

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1 purpose was to provide an opportunity, in a public
2 forum, for FDA to hear from those with experience
3 and informed opinion on the issue. We found the
4 presentations and the subsequent discussions really
5 to be very, very useful. I've taken a lot of
6 notes. I know others have taken notes. It's been
7 very useful to have this discussion. There is a
8 great deal of challenges that are still out there.

9 As a reminder, we're planning to open a
10 public docket for public comment. When that opens,
11 we'll be posting the information on the CTP
12 website, so you can also sign up for updates from
13 CTP by visiting the website. So please make sure
14 you put your comments in there. Particularly those
15 of you who didn't get a chance to speak up and add
16 to that, please add your comments there.

17 We see this workshop as an initial step.
18 This is one step along this journey. It's a very
19 complex topic, and we plan to move forward. And,
20 again, please take advantage of the public docket
21 to provide us with whatever information you have
22 that will help guide us along that way.

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1 Adjournment

2 DR. ASHLEY: So thank you all for coming.
3 We appreciate your attention and appreciate the
4 good questions and the discussion back and forth,
5 and I hope you have good travels getting back.
6 (Whereupon, at 12:50 p.m., the meeting was
7 adjourned.)

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